# School closures and influenza: systematic review of epidemiological studies


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|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID: | bmjopen-2012-002149 |
| Article Type: | Research |
| Date Submitted by the Author: | 12-Oct-2012 |


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| Complete List of Authors: | Jackson, Charlotte; London School of Hygiene and Tropical Medicine,<br>Vynnycky, Emilia; Health Protection Agency,<br>Hawker, Jeremy; Health Protection Agency,<br>Olowokure, Babatunde; Health Protection Agency,<br>mangtani, punam; London School of Hygiene and Tropical Medicine, |


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|---|---|
| <b>Primary Subject Heading</b>: | Epidemiology |
| Secondary Subject Heading: | Epidemiology, Infectious diseases, Public health |
| Keywords: | EPIDEMIOLOGY, Epidemiology < INFECTIOUS DISEASES, Public health < INFECTIOUS DISEASES, PUBLIC HEALTH, SYSTEMATIC REVIEWS |

# School closures and influenza: systematic review of epidemiological studies

Charlotte Jackson[1], Emilia Vynnycky[2], Jeremy Hawker[3], Babatunde Olowokure[3], Punam Mangtani[1]

[1] London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK; [2] Health Protection Agency, Colindale, London NW9 5EQ, UK; [3] Health Protection Agency, 5 St Philips Place, Birmingham B3 2PW, UK

Corresponding author: Charlotte Jackson, Room 113, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT.

Email: charlotte.jackson@lshtm.ac.uk

Tel: +44 (0) 207 927 2209

Word count: 3540

*Abstract*

Objective: To review the effects of school closures on pandemic and seasonal influenza outbreaks.

Design: Systematic review.

Data sources: Medline and Embase, reference lists of identified articles, hand searches of key journals, and additional papers from the authors' collections.

Study selection: Studies were included if they reported on a seasonal or pandemic influenza outbreak coinciding with a planned or unplanned school closure.

Results: Of 2579 papers identified through Medline and Embase, 65 were eligible for inclusion in the review along with 13 identified from other sources. Influenza incidence frequently declined after school closure. The effect was sometimes reversed when schools reopened, supporting a causal role for school closure in reducing incidence. Any benefits associated with school closure appeared to be greatest amongst school-aged children. However, as schools often closed late in the outbreak or other interventions were used concurrently, it was sometimes unclear how much school closure contributed to the reductions in incidence.

Conclusions: School closures appear to have the potential to reduce influenza transmission, but the heterogeneity in the data available means that the optimum strategy (e.g. the ideal length and timing of closure) remains unclear.

## *Introduction*

During the 2009 influenza pandemic, schools were closed in many settings in efforts to reduce transmission. The World Health Organization does not specifically recommend or discourage school closures during an influenza pandemic, as their potential benefits and harms may be context-specific [1], but has suggested that they be considered as part of a mitigation strategy [2]. Their effects on transmission are, however, still poorly understood [3 4]. Closures may be either pro-active (occurring before transmission is established in the school) or reactive (a response to a school-based outbreak), and may involve closure of whole school(s) or dismissal of individual classes [4].

A review of the evidence available before the 2009 pandemic concluded that school closures may be beneficial, depending on characteristics such as age-specific attack rates [4]. Here, we review epidemiological studies to assess the effects of school closures on transmission and incidence of seasonal and pandemic influenza, updating and extending previous reviews [2 4] to include data from the 2009 pandemic.

## *Methods*

### *Search strategy and selection criteria*

Medline and Embase were searched in January 2012, without language restrictions, for relevant papers published by the end of 2011 (see Appendix for search strategy). *Eurosurveillance* (23 April 2009 to 15 December 2011), *Morbidity and Mortality Weekly Report* (24 April 2009 to 23 December 2011) and *Emerging Infectious Diseases* (April 2009 to December 2011) were hand searched. Results were also supplemented with papers from the reference lists of the articles identified, and papers from the reviewers' collections. An additional search of Pubmed (for the words "influenza" and "school") was used to identify relevant papers published during October – December 2011 which were not yet listed in Medline or Embase.

Studies were included if they described one or more influenza outbreaks during which schools were initially open and subsequently closed on specified dates, with or without other interventions. If papers presented several measures of influenza activity, the most specific data were extracted (e.g. data on laboratory-confirmed influenza were extracted in preference to all-cause school absenteeism). English translations (where available) of the titles and abstracts of papers written in other languages were screened, but these papers were not eligible for inclusion.

Abstracts and full text were screened initially by one reviewer and by a second reviewer if necessary. Box 1 summarises the information extracted from the studies. Where possible, epidemic curves were plotted by transcribing daily or weekly data from figures or tables.

*Data analysis*

We plotted the peak and cumulative attack rates (and 95% confidence intervals, calculated using standard methods for calculating CIs for proportions) for each study that provided an appropriate denominator. We calculated the normalised peak (peak AR / median AR) for datasets with a median AR greater than zero, to adjust approximately for differences in case definitions (this approach has been used elsewhere to adjust for intercity differences in case fatality proportions [5]). These estimates were stratified by the timing of closure, i.e. whether schools closed before, coincident with, or after the peak.

### *Results*

Of 2579 papers identified through Medline and Embase, 430 were reviewed in full. 65 of these studies were included in the review, along with 13 additional papers (Figure 1; the supplementary PubMed search yielded no further eligible articles). 78 papers were thus included in the review: 22 for seasonal and 56 for pandemic influenza (49, one, and six from the 2009, 1968 and 1918 pandemics, respectively). Details of the studies are given in Table 1 and Supplementary Tables 1 and 2.

*Description of the epidemics*

19 and 41 epidemic curves were available on seasonal and pandemic influenza, respectively (Supplementary Figures 1 and 2). School closure was often followed by a reduction in incidence, in children specifically or in the general population. However, closure often occurred late in the outbreaks (Table 1), and it is unclear whether it influenced the decline.

The cumulative and peak ARs varied widely for seasonal and pandemic influenza (Figure 2). Normalised peaks partly account for differences in case definitions between studies, but also varied considerably (Figure 3). There was no clear pattern in the cumulative, peak or normalised peak ARs plotted by timing of closure in relation to the peak. Relatively few schools closed before the peak (Figures 2 and 3); of those that did, two also reopened before the peak [6 7]. However, early introduction of non-pharmaceutical interventions (NPIs), which often included school closures, in US cities during the 1918 influenza pandemic has been found to be associated with a reduction in mortality [5 8 9].

*Age-specific effects of school closure*

The available age-specific data suggested that any benefits associated with school closure were greatest amongst school-aged children [10-24]. In New Zealand during the 2009 pandemic, the age-standardised proportion of confirmed cases in 5-19 year olds fell during the winter holiday and increased when schools reopened [18]; a slight increase in ILI consultation rates when schools reopened was confined to 5-14 year olds [13]. Similar relationships between school closure and the ratio of the number of H1N1 infections in 5-20 year olds to that in other age groups were reported for Mexico [22] and Peru [25]. During the 1967-68 influenza season in Great Britain, GP consultation rates for ILI amongst 5-14 year-olds declined during the Christmas holiday and increased when schools reopened; this effect was less clear in other age groups [16].

Winter holidays in Israel were associated with a reduction in the ratio between the number of clinic visits for influenza and those for non-respiratory complaints, in 6-12 year olds, in three of five seasonal influenza periods studied [14]. In one season, this ratio was also reduced in adults, and in another it was reduced for adults not living with 6-12 year-olds. When a two-week teachers' strike coincided with an influenza outbreak in January 2000, closing 80% of elementary schools nationwide, this ratio decreased by 15% for 6-12 year-olds (95% CI 6-23%), but not for older individuals. As the authors note, children comprise a high proportion (34%) of the Israeli population, which may contribute to any apparent benefit of closing schools in Israel [26].

Similar data from four influenza seasons in Arizona are less consistent, partly because school closure rarely coincided with elevated influenza activity [17]. During all four seasons, rates of laboratory-confirmed influenza in school-aged children were similar during the two week winter holiday and the preceding two weeks. In two seasons this rate increased in the two weeks after schools reopened; in one other season, it was significantly lower on reopening than during closure [17]. In comparison, rates in adults and pre-school-aged children increased successively (though not always significantly) across the three two-week periods in three of the seasons [17].

Three studies which fitted transmission models to surveillance data also concluded that school closures mainly benefit children [11,12]. Analyses of French seasonal ILI data [12] and ILI data from London during the 2009 pandemic [21] estimated that school holidays did not affect adults' contact patterns; similarly, reductions in transmission following school closures in Hong Kong in 2009 occurred primarily amongst children [11].

However, two studies of the 2009 pandemic suggested that school closure affected incidence in adults. One of these studies estimated the age-specific number of ILI cases due to pandemic H1N1 in England; in most age groups, these estimated case numbers decreased during the summer holiday and increased when schools reopened [24]. In Vojvodina, Serbia, incidence decreased amongst 5-14 and 15-64 year olds during a one-week school closure [27].

*Reversibility of effects*

Incidence sometimes rebounded when schools reopened, suggesting that school closure contributed to reducing incidence in some settings. For example, during the 2009 pandemic in England, the estimated weekly number of infections declined during the school summer holiday; a second wave occurred when schools reopened (Supplementary Figure 2) [21,28]. Similar reversibility appeared in ILI consultation rates in Vojvodina in 2009 [27]. Datasets from the 2009 pandemic in Mexico [22,29,30] also suggested an increase in incidence after schools reopened (Supplementary Figure 2). Analyses of NPIs (usually including school closures) during the 1918 pandemic found that, in the cities studied, second waves occurred only after NPIs were lifted [5 8].

In the Israeli data regarding seasonal influenza and the teachers' strike, the number of physician visits for acute respiratory illness was 42% lower during the closure compared to the previous two weeks; incidence increased after the strike [26]. During the 1999-2000 influenza season in Japan, the increase in incidence appeared to slow during the two week winter holiday and accelerated when schools reopened [7]. Similarly, in Beijing in 2009, the cumulative incidence of laboratory-confirmed H1N1 influenza increased more markedly before and after a national school holiday than during the break [31].

*Changes in transmission patterns from modelling analyses of epidemic data*

Several studies have fitted transmission models to observed epidemic data to estimate the reduction in contact rates associated with school closure. School holidays were estimated to reduce transmission of seasonal influenza amongst children by a median of 24% (range 20-29%), based on rates of ILI in France from 1985 to 2006, corresponding to a 16-18% reduction in total case numbers [12]. During the 2009 pandemic in London, contact amongst 5-14 year olds was reduced by an estimated 72% during the six-week summer holiday; the corresponding reduction during one-week half term holidays was 48% [21]. In US cities in 1918, changes in mortality were attributed to a combination of formal interventions (including school closure) and spontaneous social distancing [8]. In Sydney in 1918, formal and spontaneous social distancing together were estimated to have reduced contact rates by up to 38% [32]. Based on influenza incidence data from the 2009 pandemic in Mexico City, school closure together with other interventions appeared to reduce the population contact rate by

23% [30]. A subsequent analysis of national data from Mexico estimated that the contact rate was reduced by 30% during the intervention period [22].

In Hong Kong (also during the 2009 pandemic), closing primary schools, kindergartens, and childcare centres pro-actively, together with affected secondary schools, was estimated to reduce transmission by 70% amongst children and 25% in the population overall [11]. The same study estimated the effective reproduction number ($R_n$, the average number of secondary infectious persons generated by a single infectious person in a given population) as 1·7 before school closure, 1·5 during school closure, and 1·1 during the subsequent school holidays [11]. Daily estimates of $R_n$ in Hong Kong in 2009 (based on a longer time series) also suggested a decline during school closure and a slight increase following reopening [33].

Modelling techniques have also been used to estimate daily values of $R_n$ during a seasonal influenza outbreak in Hong Kong [34] and the 2009 pandemic in Mexico City [22 30] and New Zealand [18]. The Hong Kong analysis for seasonal influenza suggested that $R_n$ was not substantially affected by school closure, perhaps because closure occurred late in the outbreak when $R_n$ was already below one [34]. In Mexico City [30] and New Zealand, $R_n$ was declining before schools closed and continued to decrease during closure; in New Zealand, $R_n$ increased briefly but not substantially when schools reopened [18]. Analysis of a further outbreak in the USA detected no clear effect of school closure on transmission, which was attributed to the late timing of closure [19].

Modelling analyses of the spatiotemporal spread of pandemic H1N1 in Europe in 2009 were able to reproduce observed incidence patterns only when contact rates were allowed to change specifically during each country's school holidays (holidays were assumed to eliminate transmission in schools and increase community transmission by a factor of 1.4) [35]. In all countries, holidays were estimated to delay the peak compared to a hypothetical situation without school closure. In contrast, regression analysis of estimates of $R_n$ in 12 European countries found no evidence of an effect of school holidays on transmission in the nine countries in which school holidays coincided with the study period [36]. The authors proposed that this apparent lack of effect might result from changes in reporting, stochastic effects early in the outbreaks, and the fact that in some countries (including England), school holidays occurred outside the study period.

*Different school closure strategies*

In some outbreaks, individual schools were closed; in others, school closure was more widespread (Supplementary Tables 1 and 2). The effects of these different strategies could not be compared, due to both late implementation and differences between the studies in other factors (such as the duration of closure).

Analyses of the 1918 pandemic in US cities found that the duration of NPIs was negatively associated with the total excess death rate [9]. In the datasets reviewed here, closures longer than two weeks were associated with reduced incidence or transmission in several studies of seasonal [37] and pandemic [11 28] influenza, but not in others [10 38]. Two studies which suggested reasonably strong evidence of an effect of school closure (from France and Israel) reported on closures lasting two weeks [12 26]. Studies in Japan [7] and England and Wales [16] also suggested possible effects of two-week closures on seasonal influenza. However, closures of this length did not always appear to reduce transmission [34]. Shorter closures, e.g. of 1-2 weeks, may sometimes have contributed to reductions in transmission [21 28 30 31 39], but often had no obvious effect [40-43]. In London, contacts between children were reduced more dramatically during a six-week holiday than during one-week breaks, but this may reflect different behaviour during the different holidays [21].

*Use of multiple interventions*

In most of the pandemic influenza studies, other interventions were implemented alongside school closure and may have contributed to any reduction in incidence. In 2009, antiviral treatment and / or prophylaxis was commonly used in the studies identified [11 13 18 19 38 39 41 44-56]. Public places were sometimes closed and / or large gatherings were discouraged or restricted [15 29 30 57]. Some datasets from the 2009 pandemic included vaccination against the pandemic strain, although this was usually only available late in the study period so would not affect the included incidence data [28 31 56 58]. In 1918, school closures were often combined with other social distancing measures [5 8 9 32]; the only study included from the 1968 pandemic was a vaccine trial [59]. Of the few pandemic studies which mentioned no additional interventions, one suggested an effect of school closures: in Israel in 2009, three waves of infection corresponded to the planned closure and reopening of schools [60]. In the England and Wales data for the 2009 pandemic, other interventions (vaccination and antivirals) were used to only a limited extent; incidence still clearly declined during the school summer holiday and increased afterwards [28].

Some studies of seasonal influenza mentioned additional interventions (e.g. vaccination [61-63], prophylactic amantadine [64], hygiene promotion [37 40 65], closure of public places [37], and advice to avoid large gatherings [43]). However, some studies without additional interventions showed reductions in incidence and / or transmission during school closure [12 26].

***Discussion***

This systematic review of the effects of school closures on influenza outbreaks extends previous reviews [2 4] to include published experiences from the 2009 pandemic. The results suggest that school closure can reduce transmission of pandemic [11] and seasonal [12 26] influenza amongst schoolchildren. Many datasets, however, show no clear effect of school closure. As noted by some authors [19 42 43], this may sometimes have been because schools shut late in the outbreak (often close to or after the peak).

In some studies, incidence increased when schools reopened [5 7 8 13 21 26 28 30]. This apparent reversibility provides evidence that school closure can cause reductions in influenza incidence. In two of the studies of seasonal influenza which showed reversibility [7 26], no additional interventions (beyond usual seasonal interventions) were used. In many other datasets, multiple interventions were used, so the specific effects of school closures are difficult to isolate.

The long term effects of closing schools are unclear, as relatively few of the studies presented substantial data after schools reopened. For example, school closure could result in multiple peaks, potentially involving more cases than would otherwise have occurred [8]. However, a study published since this review was conducted estimated that case numbers in Alberta, Canada, could have been up to twice as high as those seen if schools had not closed for planned holidays [66]. It is difficult to compare reactive versus pro-active closures, different durations of closure, and local versus national closures as studies typically differed in several respects. Age-specific data suggest that the effects of school closure are greatest among school-aged children [11-14 16 21].

Some studies have concluded that reopening schools after holiday periods can accelerate epidemic growth (e.g. during the 1957 [67 68] and 2009 [69] pandemics). These studies were beyond the scope of this review of the effects of closing schools after outbreaks have started, but they suggest that extending school holidays might delay the spread of an epidemic beginning during a break.

Results from analyses of seasonal influenza may not be directly applicable to a pandemic. Schools were often closed for planned holidays rather than in response to the outbreaks; contact patterns may differ between reactive school closures [70] and holidays [71]. Extrapolating from previous pandemics may also be problematic. Modelling studies [72-74] have predicted that school closures will have the greatest effects if transmission occurs mainly amongst children. The importance of children in transmission has varied between pandemics [75]; in 2009, attack rates were higher in children than in adults, probably because of pre-existing immunity in older individuals [76]. Viral virulence will also influence individuals' responses to school closure and other interventions, e.g. spontaneous social distancing during a mild pandemic may be less dramatic than occurred in 1918. Changes in household size, contact patterns, children's behaviour and school systems since 1918, 1957 and 1968 may also limit the generalisability of experiences from these pandemics.

One limitation of the datasets is that ascertainment may have changed during the outbreaks, due to changes in surveillance and care-seeking behaviour. Increases in ascertainment during an outbreak could obscure any reductions in incidence during school closures (e.g. in one study, enhanced surveillance began the day the school closed [55]). Conversely, the proportion of patients who undergo virological testing may be reduced late in an outbreak, and in some settings (e.g. New Zealand [13]) patients with ILI were discouraged from consulting GPs during the 2009 pandemic. The estimated proportion of influenza cases that were reported in Hong Kong declined to ~5% of its original value during the move from containment to mitigation during the 2009 pandemic [11]. In England, the introduction of the National Pandemic Flu Service telephone helpline coincided with the school holiday, and was estimated to have reduced the probability of GP consultation for adults with ILI from 16% to 1.8% [21].

Case definitions may not always have been well-suited to detecting any effect of school closure. For example, school absenteeism is a relatively non-specific measure, whilst laboratory specimens frequently represent severe infections (e.g. in the elderly, who may have little contact with children and therefore be relatively unaffected by school closure).

Previous studies have attempted to estimate the effects of public health interventions using transmission models [8 11 19 30]. The development of such models is complicated for the datasets reviewed here, and would not necessarily have provided conclusive insight into the impact of school closures. For example, many factors are unknown and would need to be estimated or assumed for each dataset, such as the basic reproduction number, proportion of infections that were reported, the effect of other interventions, and the proportion of individuals who were immune at the start of the outbreak.

The review was limited to published studies, which could potentially introduce publication bias. However, many of the studies identified did not aim to evaluate the effects of school closure on transmission, so publication bias appears unlikely. This is supported by the apparent lack of an effect of school closure in many of the studies (including some of those which did specifically assess school closure as an intervention). Foreign language papers were excluded, but in most cases it was clear from the title and / or abstract (available in English) that the papers were not relevant to this review.

***Conclusions***

The available data suggest that school closures can potentially reduce transmission during an influenza outbreak, even in the absence of other interventions, although the optimal school closure strategy is unclear. The effect of school closures is larger for school-aged children than for other age groups, although there is some evidence that incidence in adults might also be reduced. During a future pandemic (or seasonal outbreaks during which schools are closed), it will be important to collect incidence data using systematic ascertainment and a consistent case definition, before, during and after school closure, to assess the effects of school closures on transmission. Analysis of comparable data from multiple outbreaks may help to overcome some of the problems with comparability and ascertainment discussed above, and clarify which features determine the effectiveness of school closures. Although timely school closures may reduce transmission, other implications of school closure (e.g. ethical and economic considerations) [4], and viral properties such as virulence, must also be considered in policy decisions, and may depend on the local context [1].

**_Summary_**

*Article focus*

- This systematic review assesses the effects of school closures on transmission of influenza, including data from the recent 2009 pandemic as well as from previous pandemics and seasonal outbreaks.

*Key messages*

- The available data suggest that school closure can be a useful intervention during influenza outbreaks, with the greatest benefits occurring amongst school-aged children.

*Strengths and limitations*

- We have reviewed an extensive body of literature on the effects of school closure on the incidence and transmission of influenza.
- The optimum timing and duration of closure are unclear because studies often differed in several respects, or used other interventions in addition to school closure.

*Acknowledgements*

This paper developed from a review commissioned by the UK Health Protection Agency as part of its pandemic influenza programme. We thank Nadia Inglis, Angus Nicoll and two anonymous members of the HPA's Influenza and Respiratory Virus Programme Board for helpful comments on the review. We also thank staff at the LSHTM library for assistance in locating papers.

*Funding*

This work was partially funded by the Health Protection Agency; C.J. was supported by a Research Training Fellowship from the National Institute for Health Research.

*Role of the funding source*

NIHR had no role in the design and conduct of the study; collection, analysis or interpretation of data; writing of the report; or the decision to submit the article for publication. The HPA commissioned the research.

*Access to data*

All authors had full access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

*Data sharing*

No additional data available.

*Competing interest statement*

All authors have completed the Unified Competing Interest form at http://www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: funding from NIHR and HPA; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

*Statement of authors' roles*

B.O and J.H. had the initial idea. P.M., C.J. and E.V. developed the research questions and study design. C.J. carried out the literature review and P.M. assessed any doubtful papers. C.J., P.M. and E.V. analysed data. C.J., P.M. and E.V. wrote the paper. J.H. commented on outputs and contributed to the final draft. J.H. and B.O. contributed to the final draft.

*Ethical approval*

Not required.

***References***

1. World Health Organization. Reducing transmission of pandemic (H1N1) 2009 in school settings. A framework for national and local planning and response, 2009.
2. Bell DM, World Health Organization Writing Group. Non-pharmaceutical interventions for pandemic influenza, national and community measures. *Emerg Infect Dis* 2006;12(1):88-94.
3. Aledort JE, Lurie N, Wasserman J, Bozzette SA. Non-pharmaceutical public health interventions for pandemic influenza: an evaluation of the evidence base. *BMC Public Health* 2007;7:208.
4. Cauchemez S, Ferguson NM, Wachtel C, Tegnell A, Saour G, Duncan B, et al. Closure of schools during an influenza pandemic. *Lancet Infect Dis* 2009;9(8):473-81.
5. Hatchett RJ, Mecher CE, Lipsitch M. Public health interventions and epidemic intensity during the 1918 influenza pandemic. *Proc Natl Acad Sci U S A* 2007;104(18):7582-7.
6. Olson JG. School absenteeism during an outbreak of B/Hong Kong/5/72-like influenza virus in Taipei, Taiwan. *Southeast Asian J Trop Med Public Health* 1980;11(4):429-34.
7. Fujii H, Takahashi H, Ohyama T, Hattori K, Suzuki S. Evaluation of the school health surveillance system for influenza, Tokyo, 1999-2000. *Japanese Journal of Infectious Diseases* 2002;55(3):97-98.
8. Bootsma MC, Ferguson NM. The effect of public health measures on the 1918 influenza pandemic in U.S. cities. *Proc Natl Acad Sci U S A* 2007;104(18):7588-93.
9. Markel H, Lipman HB, Navarro JA, Sloan A, Michalsen JR, Stern AM, et al. Nonpharmaceutical interventions implemented by US cities during the 1918-1919 influenza pandemic.[Erratum appears in JAMA. 2007 Nov 21;298(19):2264]. *Jama* 2007;298(6):644-54.
10. Armstrong C, Hopkins R. An epidemiological study of the 1920 epidemic of influenza in an isolated rural community. *Public Health Reports* 1921;36(29):1671-702.
11. Wu JT, Cowling BJ, Lau EH, Ip DK, Ho LM, Tsang T, et al. School closure and mitigation of pandemic (H1N1) 2009, Hong Kong. *Emerg Infect Dis* 2010;16(3):538-41.
12. Cauchemez S, Valleron A-J, Boelle P-Y, Flahault A, Ferguson NM. Estimating the impact of school closure on influenza transmission from Sentinel data. *Nature* 2008;452(7188):750-4.
13. Baker MG, Wilson N, Huang QS, Paine S, Lopez L, Bandaranayake D, et al. Pandemic influenza A(H1N1)v in New Zealand: the experience from April to August 2009. *Euro Surveill* 2009;14(34).
14. Heymann AD, Hoch I, Valinsky L, Kokia E, Steinberg DM. School closure may be effective in reducing transmission of respiratory viruses in the community. *Epidemiol Infect* 2009;137(10):1369-76.
15. Tinoco Y, Razuri H, Ortiz EJ, Gomez J, Widdowson MA, Uyeki T, et al. Preliminary population-based epidemiological and clinical data on 2009 pandemic H1N1 influenza A (pH1N1) from Lima, Peru. *Influenza Other Respi Viruses* 2009;3(6):253-6.
16. Miller DL, Lee JA. Influenza in Britain 1967-68. *Journal of Hygiene* 1969;67:559-72.
17. Wheeler CC, Erhart LM, Jehn ML. Effect of school closure on the incidence of influenza among school-age children in Arizona. *Public Health Rep* 2010;125(6):851-9.
18. Paine S, Mercer GN, Kelly PM, Bandaranayake D, Baker MG, Huang QS, et al. Transmissibility of 2009 pandemic influenza A(H1N1) in New Zealand: effective

reproduction number and influence of age, ethnicity and importations. *Euro Surveill* 2010;15(24).

19. Cauchemez S, Bhattarai A, Marchbanks TL, Fagan RP, Ostroff S, Ferguson NM, et al. Role of social networks in shaping disease transmission during a community outbreak of 2009 H1N1 pandemic influenza. *Proc Natl Acad Sci U S A* 2011;108(7):2825-30.
20. Marchbanks TL, Bhattarai A, Fagan RP, Ostroff S, Sodha SV, Moll ME, et al. An outbreak of 2009 pandemic influenza A (H1N1) virus infection in an elementary school in Pennsylvania. *Clin Infect Dis* 2011;52 Suppl 1:S154-60.
21. Birrell PJ, Ketsetzis G, Gay NJ, Cooper BS, Presanis AM, Harris RJ, et al. Bayesian modeling to unmask and predict influenza A/H1N1pdm dynamics in London. *Proceedings of the National Academy of Sciences of the United States of America* 2011;108(45):18238-43.
22. Chowell G, Echevarria-Zuno S, Viboud C, Simonsen L, Tamerius J, Miller MA, et al. Characterizing the epidemiology of the 2009 influenza A/H1N1 pandemic in Mexico. *PLoS Med* 2011;8(5):e1000436.
23. Chowell G, Viboud C, Munayco CV, Gomez J, Simonsen L, Miller MA, et al. Spatial and temporal characteristics of the 2009 A/H1N1 influenza pandemic in Peru. *PLoS ONE* 2011;6(6):e21287.
24. Evans B, Charlett A, Powers C, McLean E, Zhao H, Bermingham A, et al. Has estimation of numbers of cases of pandemic influenza H1N1 in England in 2009 provided a useful measure of the occurrence of disease? *Influenza and other Respiratory Viruses* 2011;5(6):e504-e12.
25. Munayco CV, Gomez J, Laguna-Torres VA, Arrasco J, Kochel TJ, Fiestas V, et al. Epidemiological and transmissibility analysis of influenza A(H1N1)v in a southern hemisphere setting: Peru. *Euro surveillance : bulletin europeen sur les maladies transmissibles = European communicable disease bulletin* 2009;14(32).
26. Heymann A, Chodick G, Reichman B, Kokia E, Laufer J. Influence of school closure on the incidence of viral respiratory diseases among children and on health care utilization. *Pediatr Infect Dis J* 2004;23(7):675-7.
27. Petrovic V, Seguljev Z, Cosic G, Ristic M, Nedeljkovic J, Dragnic N, et al. Overview of the winter wave of 2009 pandemic influenza A(H1N1)v in Vojvodina, Serbia. *Croatian Medical Journal* 2011;52(2):141-50.
28. Baguelin M, Hoek AJV, Jit M, Flasche S, White PJ, Edmunds WJ. Vaccination against pandemic influenza A/H1N1v in England: A real-time economic evaluation. *Vaccine* 2010;28(12):2370-84.
29. Echevarria-Zuno S, Mejia-Arangure JM, Mar-Obeso AJ, Grajales-Muniz C, Robles-Perez E, Gonzalez-Leon M, et al. Infection and death from influenza A H1N1 virus in Mexico: a retrospective analysis. *Lancet* 2009.
30. Cruz-Pacheco G, Duran L, Esteva L, Minzoni A, Lopez-Cervantes M, Panayotaros P, et al. Modelling of the influenza A(H1N1)v outbreak in Mexico City, April-May 2009, with control sanitary measures. *Euro Surveill* 2009;14(26).
31. Wu J, Xu F, Lu L, Lu M, Miao L, Gao T, et al. Safety and effectiveness of a 2009 H1N1 vaccine in Beijing. *New England Journal of Medicine* 2010;363(25):2416-23.
32. Caley P, Philp DJ, McCracken K. Quantifying social distancing arising from pandemic influenza. *Journal of the Royal Society Interface* 2008;5(23):631-9.
33. Cowling BJ, Lau MSY, Ho LM, Chuang SK, Tsang T, Liu SH, et al. The effective reproduction number of pandemic influenza: Prospective estimation. *Epidemiology* 2010;21(6):842-46.

34. Cowling BJ, Lau EHY, Lam CLH, Cheng CKY, Kovar J, Chan KH, et al. Effects of school closures, 2008 winter influenza season, Hong Kong. *Emerg Infect Dis* 2008;14(10):1660-2.
35. Merler S, Ajelli M, Pugliese A, Ferguson NM. Determinants of the spatiotemporal dynamics of the 2009 H1N1 pandemic in europe: Implications for real-time modelling. *PLoS Computational Biology* 2011;7(9).
36. Flasche S, Hens N, Boelle P-Y, Mossong J, van Ballegooijen WM, Nunes B, et al. Different transmission patterns in the early stages of the influenza A(H1N1)v pandemic: a comparative analysis of 12 European countries. *Epidemics* 2011;3(2):125-33.
37. Lo JY, Tsang TH, Leung YH, Yeung EY, Wu T, Lim WW. Respiratory infections during SARS outbreak, Hong Kong, 2003. *Emerg Infect Dis* 2005;11(11):1738-41.
38. Gomez J, Munayco C, Arrasco J, Suarez L, Laguna-Torres V, Aguilar P, et al. Pandemic influenza in a southern hemisphere setting: the experience in Peru from May to September, 2009. *Euro Surveill* 2009;14(42).
39. Kawaguchi R, Miyazono M, Noda T, Takayama Y, Sasai Y, Iso H. Influenza (H1N1) 2009 outbreak and school closure, Osaka Prefecture, Japan. *Emerg Infect Dis* 2009;15(10):1685.
40. Danis K, Fitzgerald M, Connell J, Conlon M, Murphy PG. Lessons from a pre-season influenza outbreak in a day school. *Commun Dis Public Health* 2004;7(3):179-83.
41. Calatayud L, Kurkela S, Neave PE, Brock A, Perkins S, Zuckerman M, et al. Pandemic (H1N1) 2009 virus outbreak in a school in London, April-May 2009: an observational study. *Epidemiol Infect* 2010;138(2):183-91.
42. Rodriguez CV, Rietberg K, Baer A, Kwan-Gett T, Duchin J. Association between school closure and subsequent absenteeism during a seasonal influenza epidemic. *Epidemiology* 2009;20(6):787-92.
43. Johnson AJ, Moore ZS, Edelson PJ, Kinnane L, Davies M, Shay DK, et al. Household responses to school closure resulting from outbreak of influenza B, North Carolina. *Emerg Infect Dis* 2008;14(7):1024-30.
44. Smith A, Coles S, Johnson S, Saldana L, Ihekweazu C, O'Moore E. An outbreak of influenza A(H1N1)v in a boarding school in South East England, May-June 2009. *Euro Surveill* 2009;14(27):9.
45. Effler PV, Carcione D, Giele C, Dowse GK, Goggin L, Mak DB. Household responses to pandemic (H1N1) 2009-related school closures, Perth, Western Australia. *Emerg Infect Dis* 2010;16(2):205-11.
46. Health Protection Agency West Midlands H1N1v Investigation Team. Preliminary descriptive epidemiology of a large school outbreak of influenza A(H1N1)v in the West Midlands, United Kingdom, May 2009. *Euro Surveill* 2009;14(27).
47. Wallensten A, Oliver I, Lewis D, Harrison S. Compliance and side effects of prophylactic oseltamivir treatment in a school in South West England. *Euro Surveill* 2009;14(30):19285.
48. Strong M, Burrows J, Stedman E, Redgrave P. Adverse drug effects following oseltamivir mass treatment and prophylaxis in a school outbreak of 2009 pandemic influenza A(H1N1) in June 2009, Sheffield, United Kingdom. *Euro Surveill* 2010;15(19):pii/19565.
49. Guinard A, Grout L, Durand C, Schwoebel V. Outbreak of influenza A(H1N1)v without travel history in a school in the Toulouse district, France, June 2009. *Euro Surveill* 2009;14(27).

50. France AM, Jackson M, Schrag S, Lynch M, Zimmerman C, Biggerstaff M, et al. Household transmission of 2009 influenza A (H1N1) virus after a school-based outbreak in New York City, April-May 2009. *J Infect Dis* 2010;201(7):984-92.
51. Lessler J, Reich NG, Cummings DAT, New York City Department of H, Mental Hygiene Swine Influenza Investigation T, Nair HP, et al. Outbreak of 2009 pandemic influenza A (H1N1) at a New York City school. *N Engl J Med* 2009;361(27):2628-36.
52. Nishiura H, Castillo-Chavez C, Safan M, Chowell G. Transmission potential of the new influenza A(H1N1) virus and its age-specificity in Japan. *Euro Surveill* 2009;14(22):4.
53. Shimada T, Gu Y, Kamiya H, Komiya N, Odaira F, Sunagawa T, et al. Epidemiology of influenza A(H1N1)v virus infection in Japan, May-June 2009. *Euro Surveill* 2009;14(24).
54. Carrillo-Santisteve P, Renard-Dubois S, Cheron G, Csaszar-Goutchkoff M, Lecuit M, Lortholary O, et al. 2009 pandemic influenza A(H1N1) outbreak in a complex of schools in Paris, France, June 2009. *Euro Surveill* 2010;15(25):24.
55. Huai Y, Lin J, Varma JK, Peng Z, He J, Cheng C, et al. A primary school outbreak of pandemic 2009 influenza A (H1N1) in China. *Influenza other respi* 2010;4(5):259-66.
56. Poggensee G, Gilsdorf A, Buda S, Eckmanns T, Claus H, Altmann D, et al. The first wave of pandemic influenza (H1N1) 2009 in Germany: From initiation to acceleration. *BMC Infectious Diseases* 2010;10(155).
57. Miller JC, Danon L, O'Hagan JJ, Goldstein E, Lajous M, Lipsitch M. Student behavior during a school closure caused by pandemic influenza A/H1N1. *PLoS ONE* 2010;5(5):e10425.
58. Hsueh P-R, Lee P-I, Hsiang Chiu A-W, Yen M-Y. Pandemic (H1N1) 2009 vaccination and class suspensions after outbreaks, Taipei City, Taiwan. *Emerg Infect Dis* 2010;16(8):1309-11.
59. Monto AS, Davenport FM, Napier JA, Francis Jr T. Modification of an outbreak of influenza in tecumseh, michigan by vaccination of schookhildren. *J.Infect.Dis* 1970;122(1-2):328-32.
60. Engelhard D, Bromberg M, Averbuch D, Tenenbaum A, Goldmann D, Kunin M, et al. Increased extent of and risk factors for pandemic (H1N1) 2009 and seasonal infl uenza among children, Israel. *Emerging Infectious Diseases* 2011;17(9):1740-43.
61. Briscoe JH. The protective effect of influenza vaccine in a mixed influenza A and B epidemic in a boys' boarding school. *J R Coll Gen Pract* 1977;27(166):28-31.
62. Farley TA, St. Germain JM, Chamberlain LA, Krassner L. The impact of influenza vaccination on respiratory illness at a boarding School. *Journal of American College Health* 1992;41(3):127-31.
63. Sonoguchi T, Naito H, Hara M. Cross-subtype protection in humans during sequential, overlapping, and/or concurrent epidemics caused by H3N2 and H1N1 influenza viruses. *Journal of Infectious Diseases* 1985;151(1):81-88.
64. Davies JR, Grilli EA, Smith AJ, Hoskins TW. Prophylactic use of amantadine in a boarding school outbreak of influenza A. *J R Coll Gen Pract* 1988;38(313):346-8.
65. Cashman P, Massey P, Durrheim D, Islam F, Merritt T, Eastwood K. Pneumonia cluster in a boarding school--implications for influenza control. *Commun Dis Intell* 2007;31(3):296-8.
66. Earn DJ, He D, Loeb MB, Fonseca K, Lee BE, Dushoff J. Effects of school closure on incidence of pandemic influenza in alberta, Canada. *Ann Intern Med* 2012;156(3):173-81.

67. Brunyate WDT, Fleming GM, Llopis A, Roden AT. The early stages of the 1957 influenza epidemic in england and wales in relation to the re-assembly of schools. *Mon Bull Minist Hlth Lab Serv* 1961;20(MAY):88-92.
68. Dunn FL, Carey DE, Cohen A, Martin JD. Epdemiologic studies of asian influenza in a louisiana parish. *Amer* 1959;J.Hyg. 70(3):351-71.
69. Chao DL, Halloran ME, Longini IM, Jr. School opening dates predict pandemic influenza A(H1N1) outbreaks in the United States. *J Infect Dis* 2010;202(6):877-80.
70. Jackson C, Mangtani P, Vynnycky E, Fielding K, Kitching A, Mohamed H, et al. School closures and student contact patterns. *Emerging Infectious Diseases* 2011;17(2):245-47.
71. Eames KTD, Tilston NL, White PJ, Adams E, Edmunds WJ. The impact of illness and the impact of school closure on social contact patterns. *Health Technol Assess* 2010;14(34):267-312.
72. Glass K, Barnes B. How much would closing schools reduce transmission during an influenza pandemic? *Epidemiology* 2007;18(5):623-8.
73. Vynnycky E, Edmunds WJ. Analyses of the 1957 (Asian) influenza pandemic in the United Kingdom and the impact of school closures. *Epidemiol Infect* 2008;136(2):166-79.
74. Milne GJ, Kelso JK, Kelly HA, Huband ST, McVernon J. A small community model for the transmission of infectious diseases: comparison of school closure as an intervention in individual-based models of an influenza pandemic. *PLoS ONE* 2008;3(12):e4005.
75. Davis LE, Caldwell GG, Lynch RE. Hong Kong influenza: The epidemiologic features of a high school family study analyzed and compared with a similar study during the 1957Asian influenza epidemic. *American Journal of Epidemiology* 1970;92(4):520.
76. Miller E, Hoschler K, Hardelid P, Stanford E, Andrews N, Zambon M. Incidence of 2009 pandemic influenza A H1N1 infection in England: a cross-sectional serological study. *Lancet* 2010;375(9720):1100-8.
77. Uchida M, Tsukahara T, Kaneko M, Washizuka S, Kawa S. Swine-origin influenza a outbreak 2009 at Shinshu University, Japan. *BMC Public Health* 2011;11:79.

**Table 1:** Features of the studies identified. Studies may present more than one dataset and so appear in more than one row of each section.

| | | Number of studies |
|---|---|---|
| | ***Total studies*** | ***78*** |
| Type of outbreak | Seasonal | 22 |
| | 1918 pandemic | 6 |
| | 1968 pandemic | 1 |
| | 2009 pandemic | 49 |
| Setting | Europe | 22 |
| | North America | 21 |
| | Central America | 5 |
| | South America | 3 |
| | Asia | 20 |
| | Africa | 1 |
| | Australasia | 6 |
| Data provided on[1]: | Children only | 25 |
| | General population | 28 |
| | School pupils and staff | 5 |
| | Children and other specified groups separately | 22 |
| Reason for closure | High student absenteeism | 3 |
| | High staff absenteeism | 1 |
| | High student and staff absenteeism | 1 |
| | Other reactive closure[2] | 30 |
| | Pro-active | 7 |
| | Planned holiday | 38 |
| | Other[3] | 3 |
| | Unclear | 3 |
| Period of closure | Continuous | 67 |
| | Intermittent | 8 |
| | Variable[4] | 3 |
| Other interventions in place[5] | None | 20 |
| | Antivirals | 33 |
| | Other social distancing | 23 |
| | Vaccination | 8 |
| | Other | 20 |
| Timing of closure | Before peak | 21 |
| | Same day / week as peak | 9 |
| | After peak | 36 |
| | Variable[4] | 8 |
| | Unclear | 7 |
| Duration of closure[6] | <7 days | 8 |
| | 7-13 days | 33 |
| | 14-20 days | 19 |
| | ≥21 days | 17 |
| | Variable[4] | 6 |
| | Not stated | 1 |

[1] Each study may present more than one data source

[2] Closure in response to outbreak, not stated as being for operational reasons

[3] Teachers' strike (2 studies) or response to SARS outbreak (1 study)

[4] Studies of multiple US cities during the 1918 pandemic or multiple countries in 2009

[5] Described in the included paper or related papers; excludes normal levels of vaccine and antiviral usage in seasonal datasets.

[6] Each study may present more than one dataset for which the durations of closure differed

***Figure legends***

**Figure 1:** Identification of epidemiological studies of the effects of school closure on influenza outbreaks

**Figure 2:** Peak cumulative attack rates recorded in the identified studies. Case definitions varied between studies (see Appendix); only studies which included a denominator are shown. Studies which reported peak prevalence of absenteeism are denoted by an asterisk. See Appendix for full details of datasets. Abbreviations: BC, British Colombia; IL, Illinois; CT, Connecticut; NC, North Carolina; UK, United Kingdom; KI, Kelleys Island. All pandemic data are from 2009 except for Kelleys Island.

**Figure 3:** Normalised peak attack rates (estimated as peak attack rate / median attack rate) recorded in the identified studies; one study with an estimate normalised peak of 128 is excluded for clarity [77]. Case definitions varied between studies (see Appendix). Studies which reported peak prevalence of absenteeism are denoted by an asterisk. Abbreviations: HK, Hong Kong; IL, Illinois; SARI, severe acute respiratory infection; NC, North Carolina; UK, United Kingdom; KI, Kelleys Island.

**Box 1: Information extracted from eligible studies (where presented)**

Study design

Study population / setting (including size of population)

Nature of school closure (e.g. school holiday, response to outbreak)

Duration of closure and number of schools affected

Timing of closure in relation to influenza circulation

Outcome measure(s) examined (e.g. clinical ILI, virologically confirmed influenza)

Association between school closure and outcome

Epidemic curve (transcribed from graphs or figures); used to derive peak, cumulative and median attack rates

Normalised peak attack rate (= peak attack rate / median attack rate)

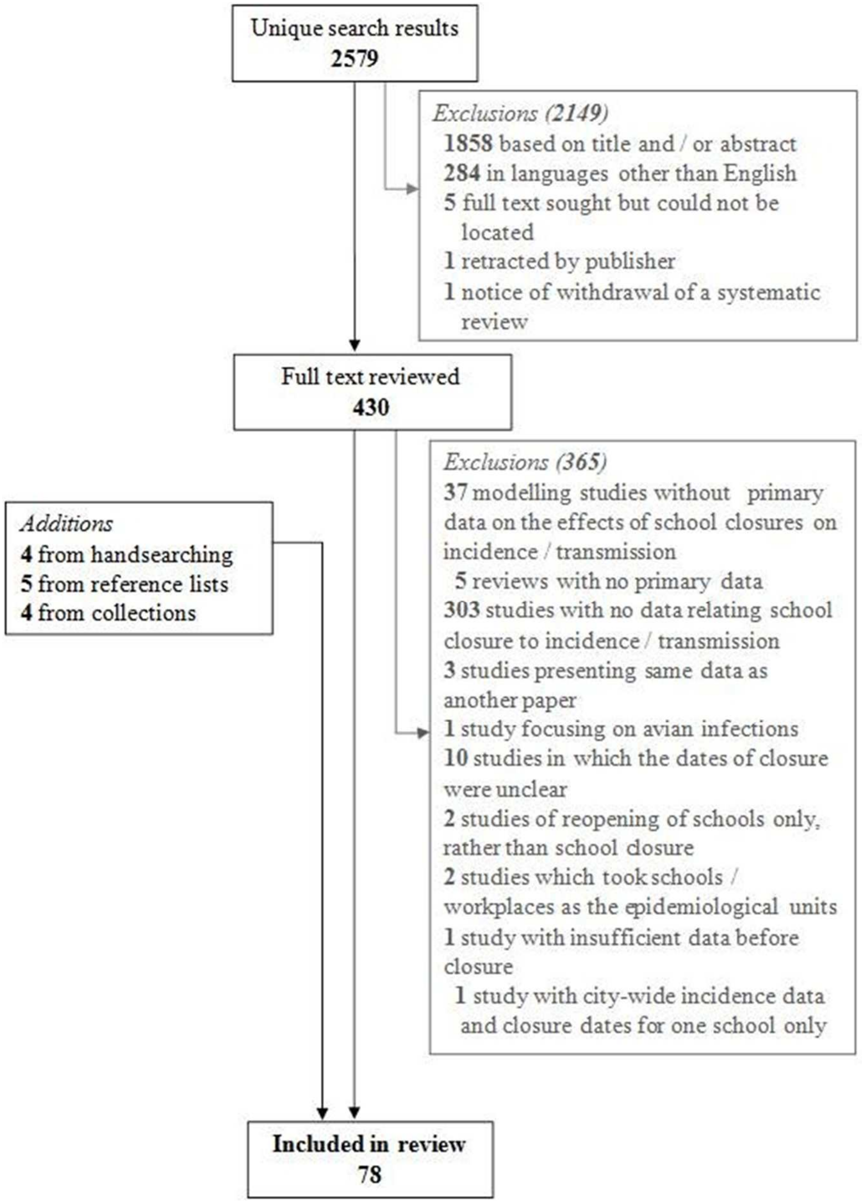



Figure 1: Identification of epidemiological studies of the effects of school closure on influenza outbreaks
147x205mm (96 x 96 DPI)

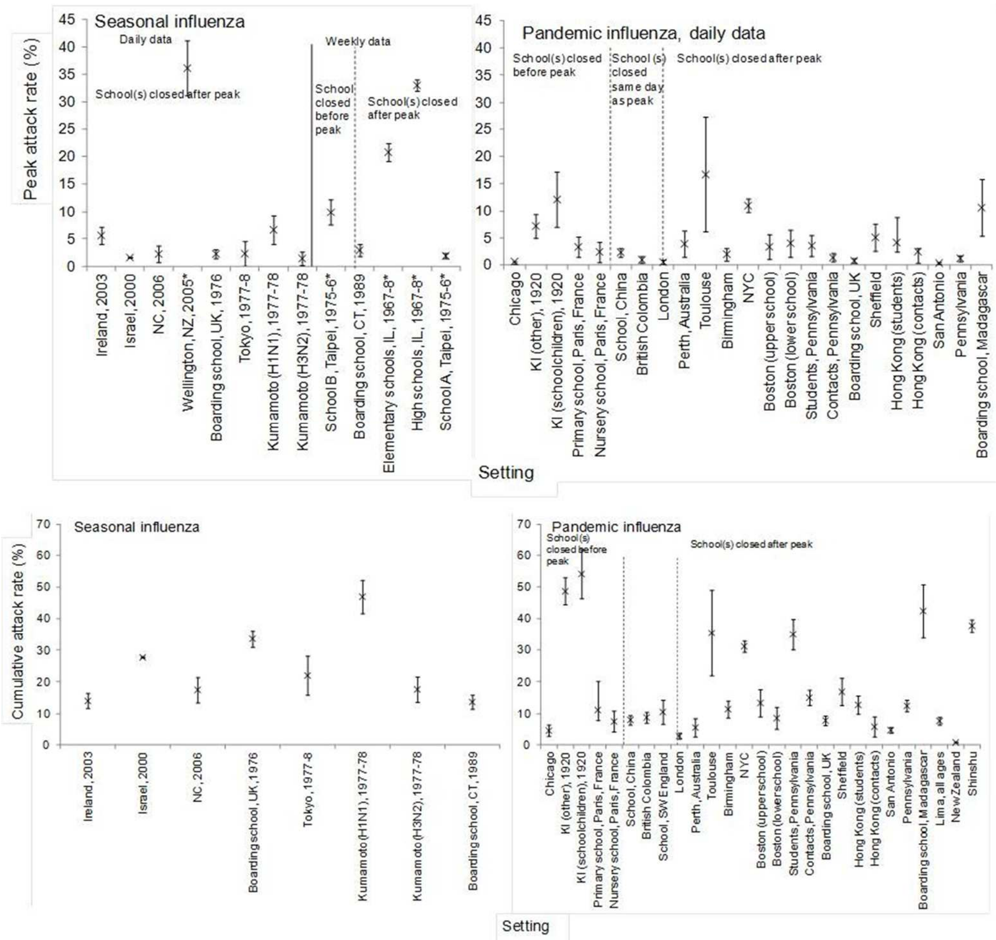



Figure 2: Peak cumulative attack rates recorded in the identified studies. Case definitions varied between studies (see Appendix); only studies which included a denominator are shown. Studies which reported peak prevalence of absenteeism are denoted by an asterisk. See Appendix for full details of datasets. Abbreviations: BC, British Colombia; IL, Illinois; CT, Connecticut; NC, North Carolina; UK, United Kingdom; KI, Kelleys Island. All pandemic data are from 2009 except for Kelleys Island.
161x152mm (150 x 150 DPI)

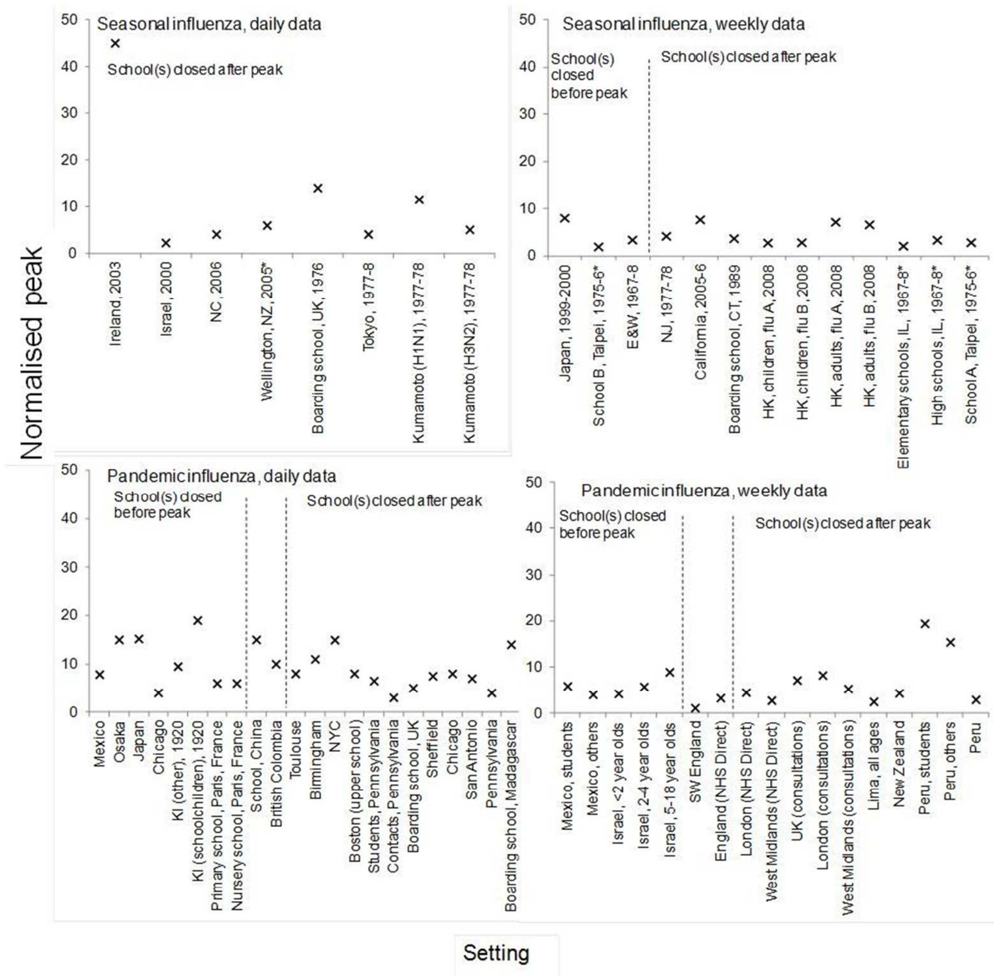



Figure 3: Normalised peak attack rates (estimated as peak attack rate / median attack rate) recorded in the identified studies; one study with an estimate normalised peak of 128 is excluded for clarity 77. Case definitions varied between studies (see Appendix). Studies which reported peak prevalence of absenteeism are denoted by an asterisk. Abbreviations: HK, Hong Kong; IL, Illinois; SARI, severe acute respiratory infection; NC, North Carolina; UK, United Kingdom; KI, Kelleys Island.
159x156mm (150 x 150 DPI)

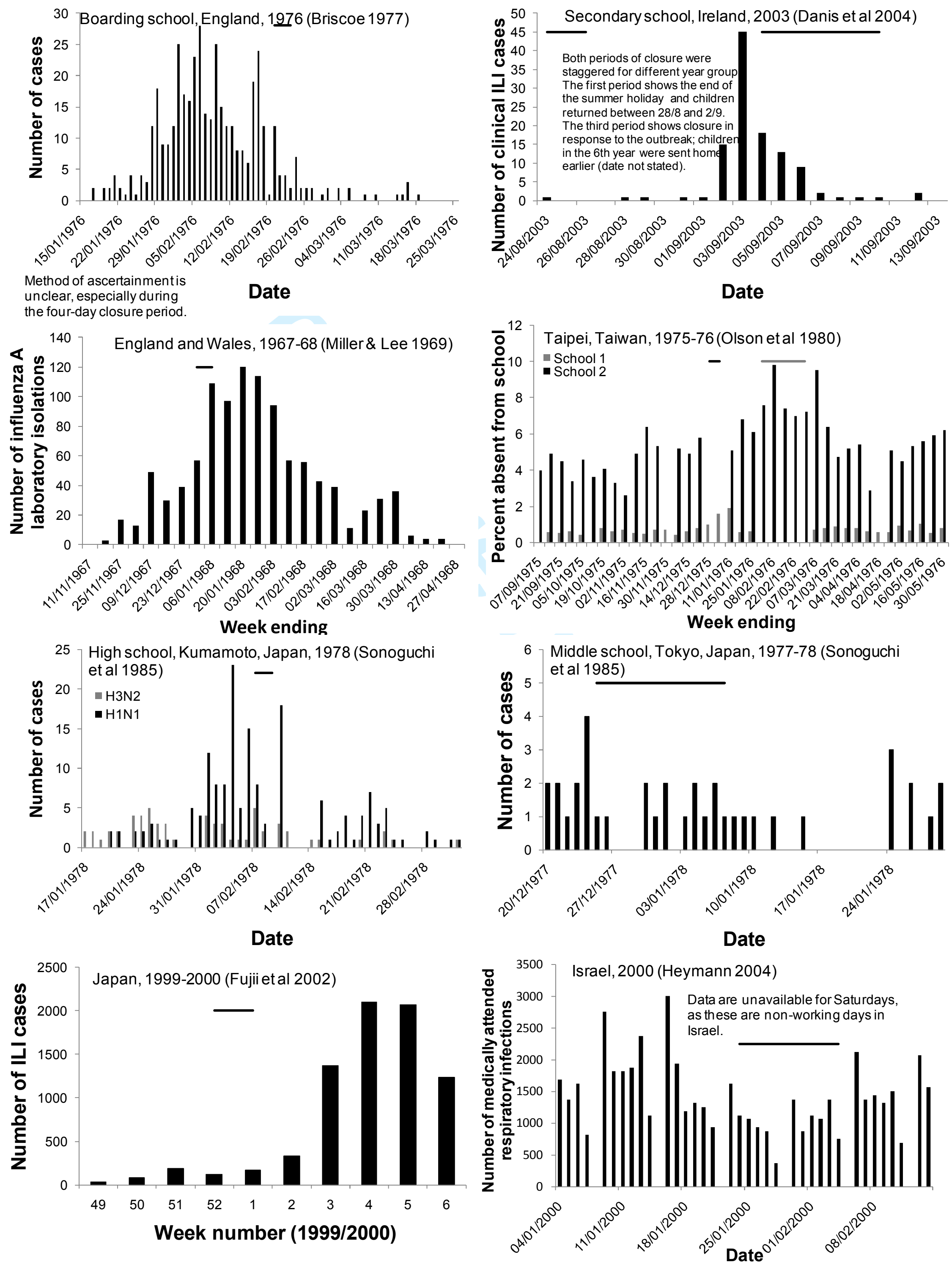
**Epidemiological evidence of the effects of school closures on influenza outbreaks: systematic review**

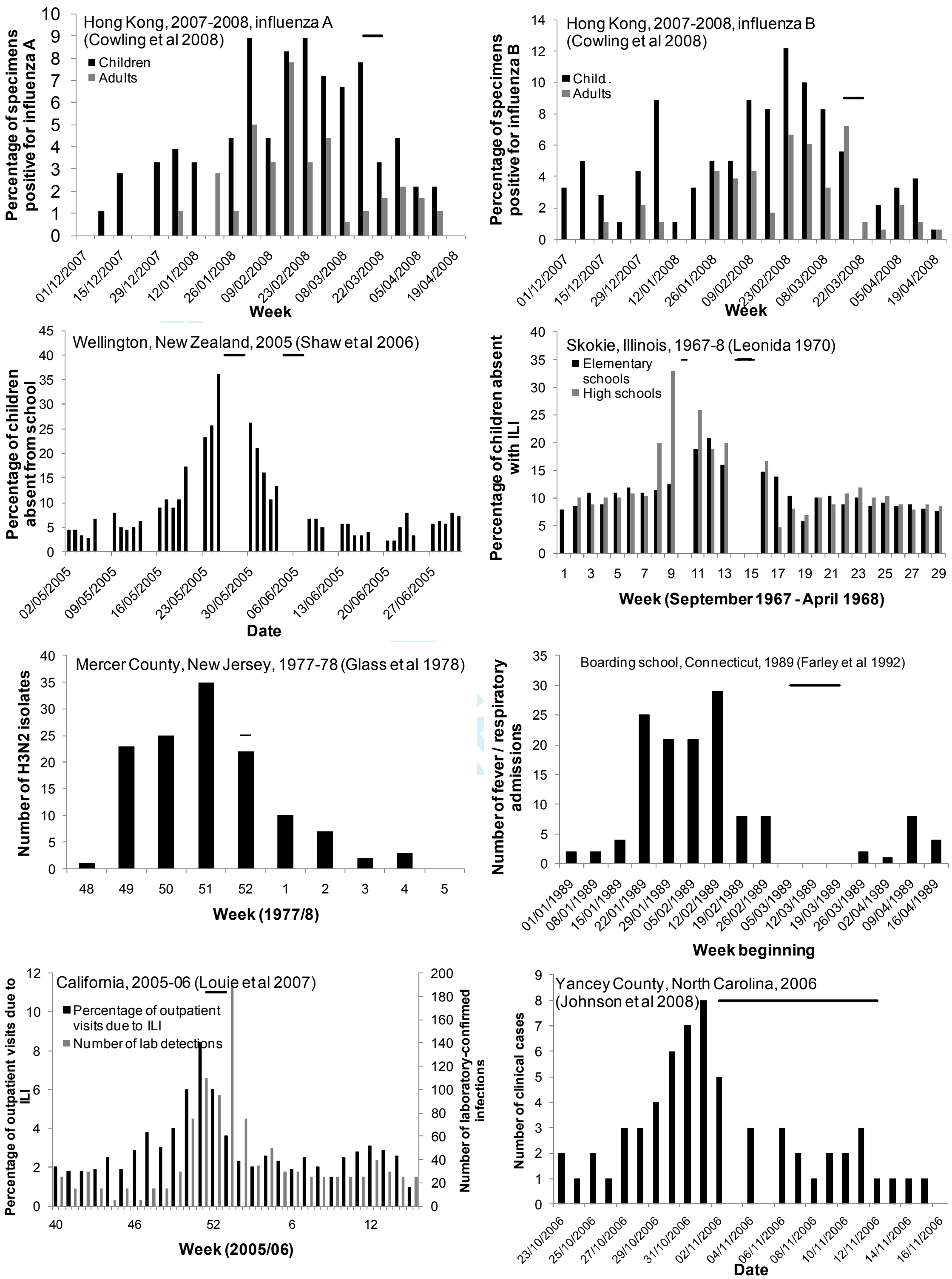
**Supplementary Information**

**Search strategy used in Medline**

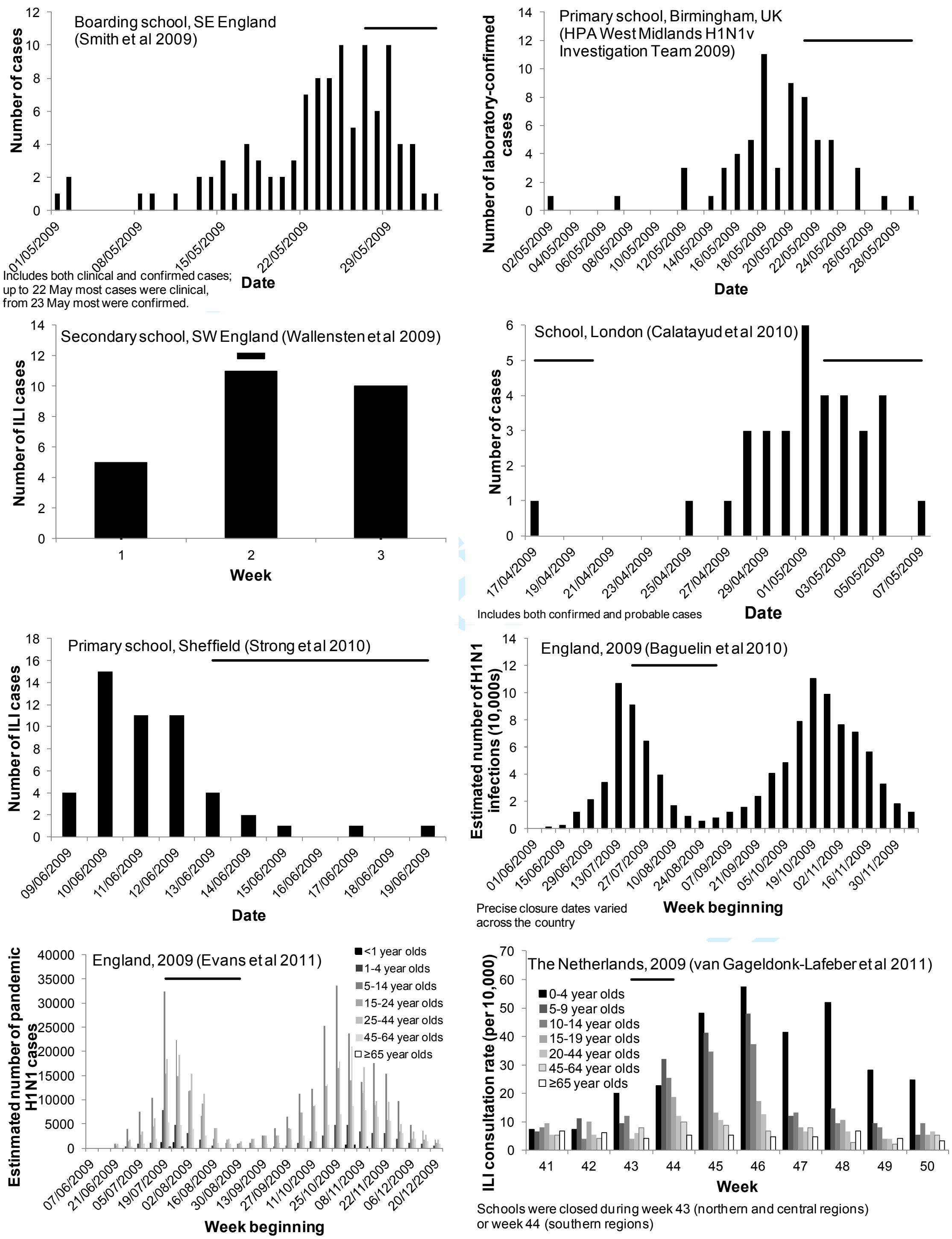
1. influenza.mp. or exp Influenza, Human/
2. exp Incidence/
3. exp Morbidity/
4. exp Sentinel Surveillance/ or exp Population Surveillance/
5. exp Disease Transmission, Horizontal/ or exp Acute Disease/ or exp Disease Notification/ or exp Disease Outbreaks/ or exp Communicable Disease Control/ or exp Disease/ or exp Disease Transmission/
6. (incidence or rate or morbidity or mortality or surveillance or risk or illness or death or case* or disease or infect*).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
7. (infect* or communicable or contagio*).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
8. exp Infection/
9. exp Communicable Diseases/ or exp Communicable Disease Control/ or exp Communicable Diseases, Emerging/
10. 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. ((school adj5 clos*) or (nurser* adj5 clos*) or (daycare adj5 clos*) or (day adj care adj5 clos*)).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
12. exp Schools/
13. 11 or 12
14. 1 and 10 and 13

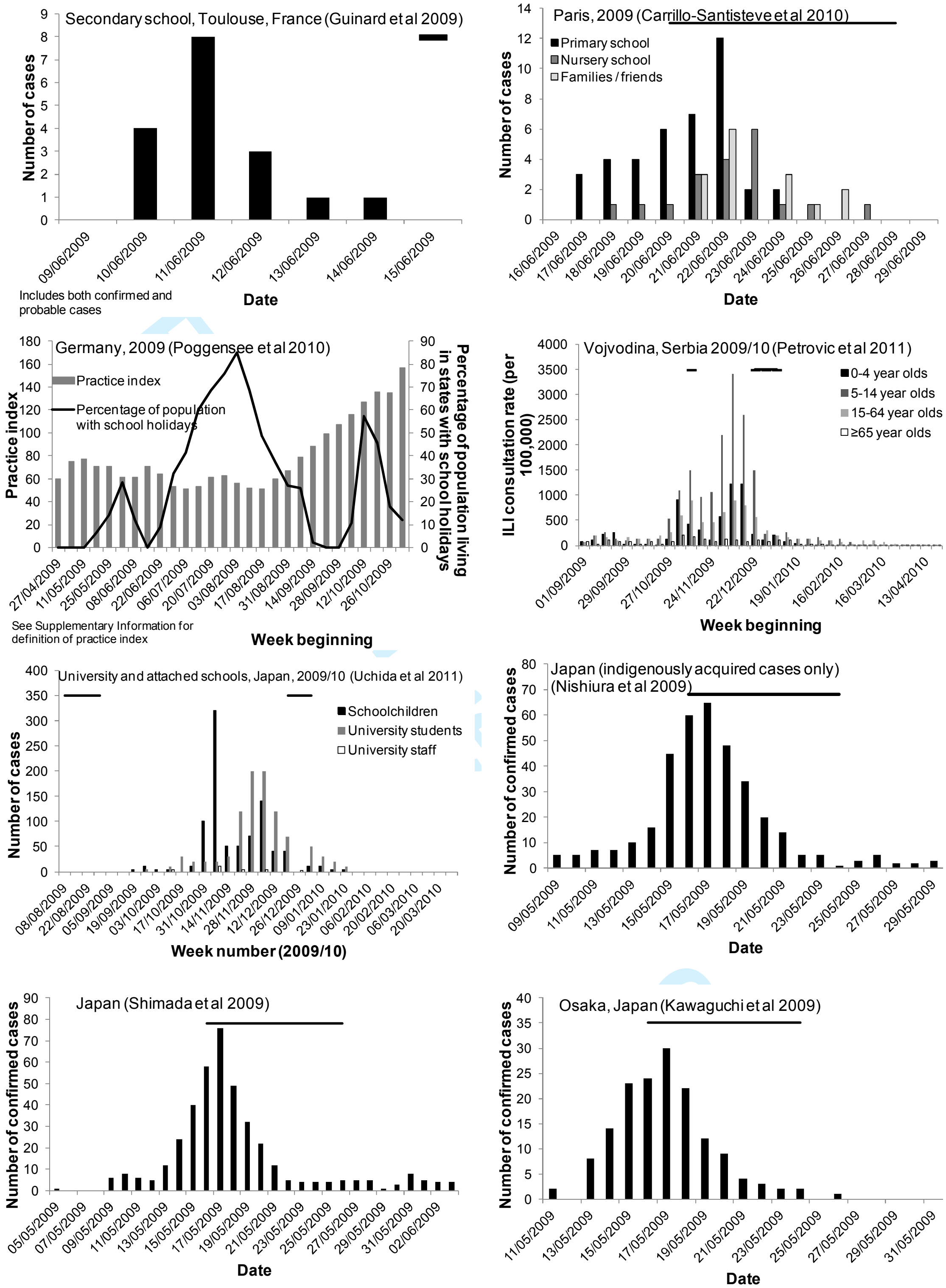
**Supplementary Figure 1: Epidemic curves for seasonal influenza. Horizontal lines show periods of school closure (weekends are shown only if they are continuous with periods of pro-active or reactive closure). Data are daily unless the x axis indicates otherwise. See eTable 1 for case definitions and full details of the datasets.**



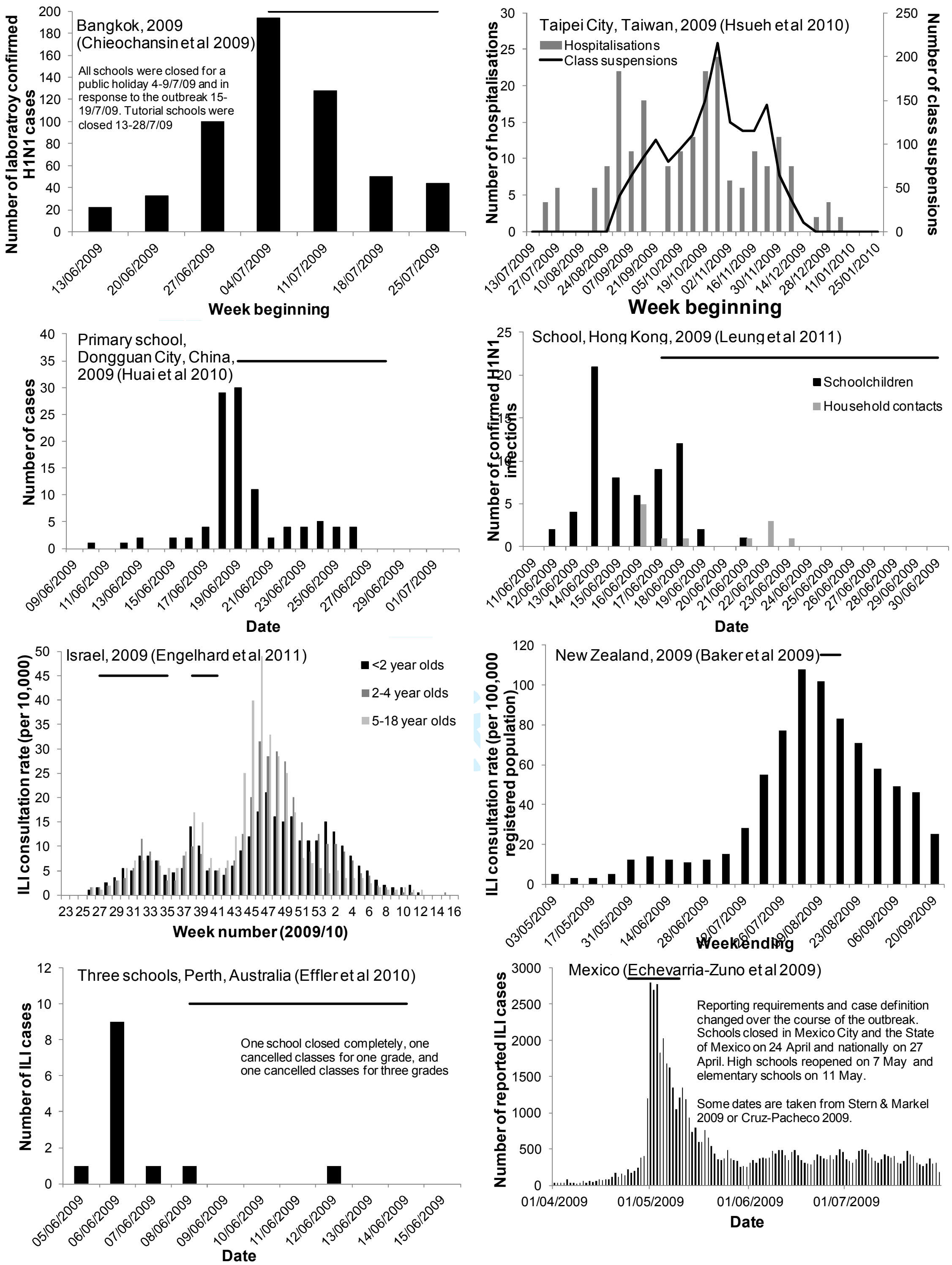

Hong Kong, 2007-2008, influenza A (Cowling et al 2008)
Hong Kong, 2007-2008, influenza B (Cowling et al 2008)
Wellington, New Zealand, 2005 (Shaw et al 2006)
Skokie, Illinois, 1967-8 (Leonida 1970)
Mercer County, New Jersey, 1977-78 (Glass et al 1978)
Boarding school, Connecticut, 1989 (Farley et al 1992)
California, 2005-06 (Louie et al 2007)
Yancey County, North Carolina, 2006 (Johnson et al 2008)

**Supplementary Figure 2: Epidemic curves for pandemic influenza. Horizontal lines show periods of school closure (weekends are shown only if they are continuous with periods of pro-active or reactive closure). See eTable 2 for case definitions and full details of the datasets.**

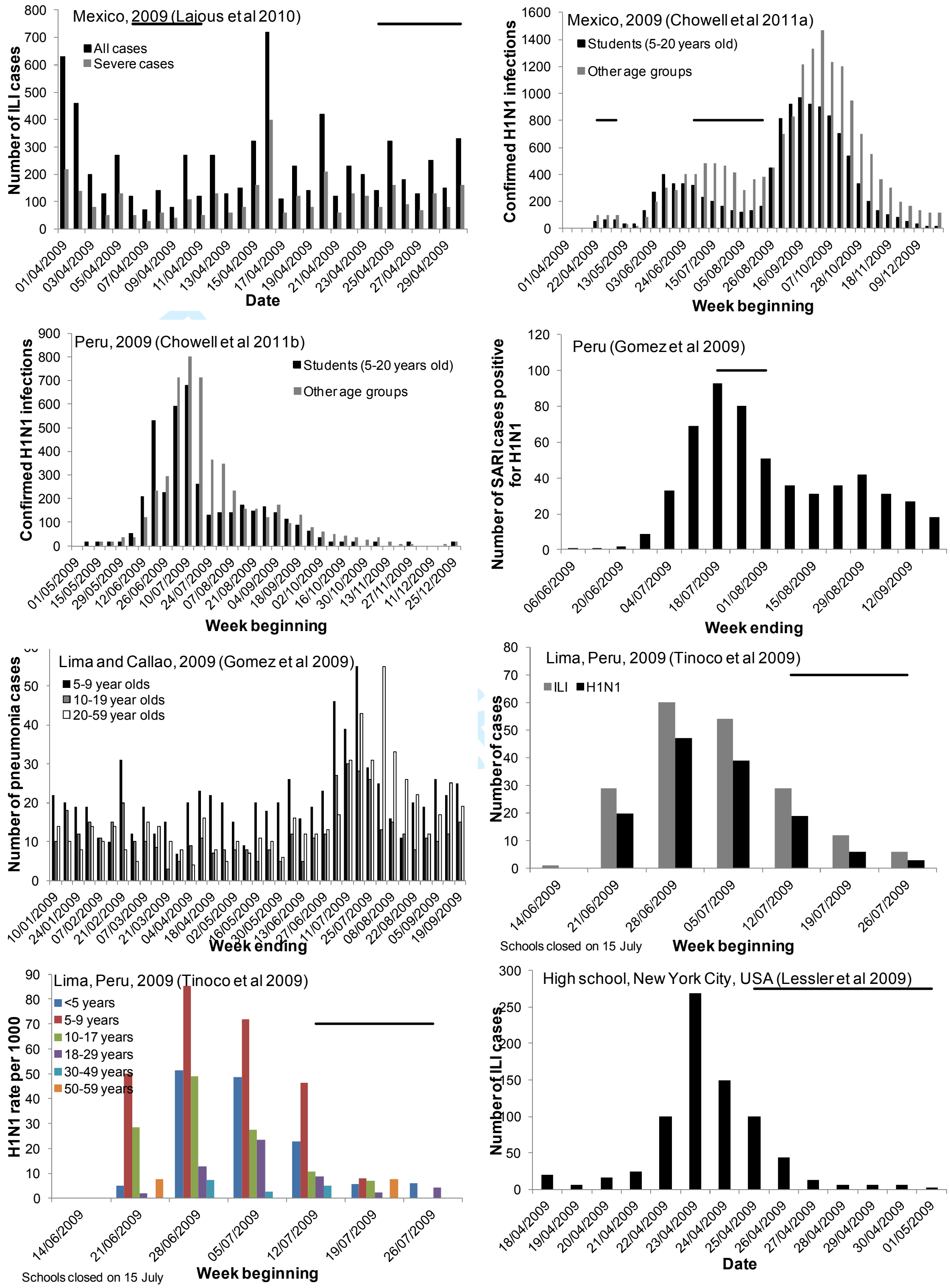


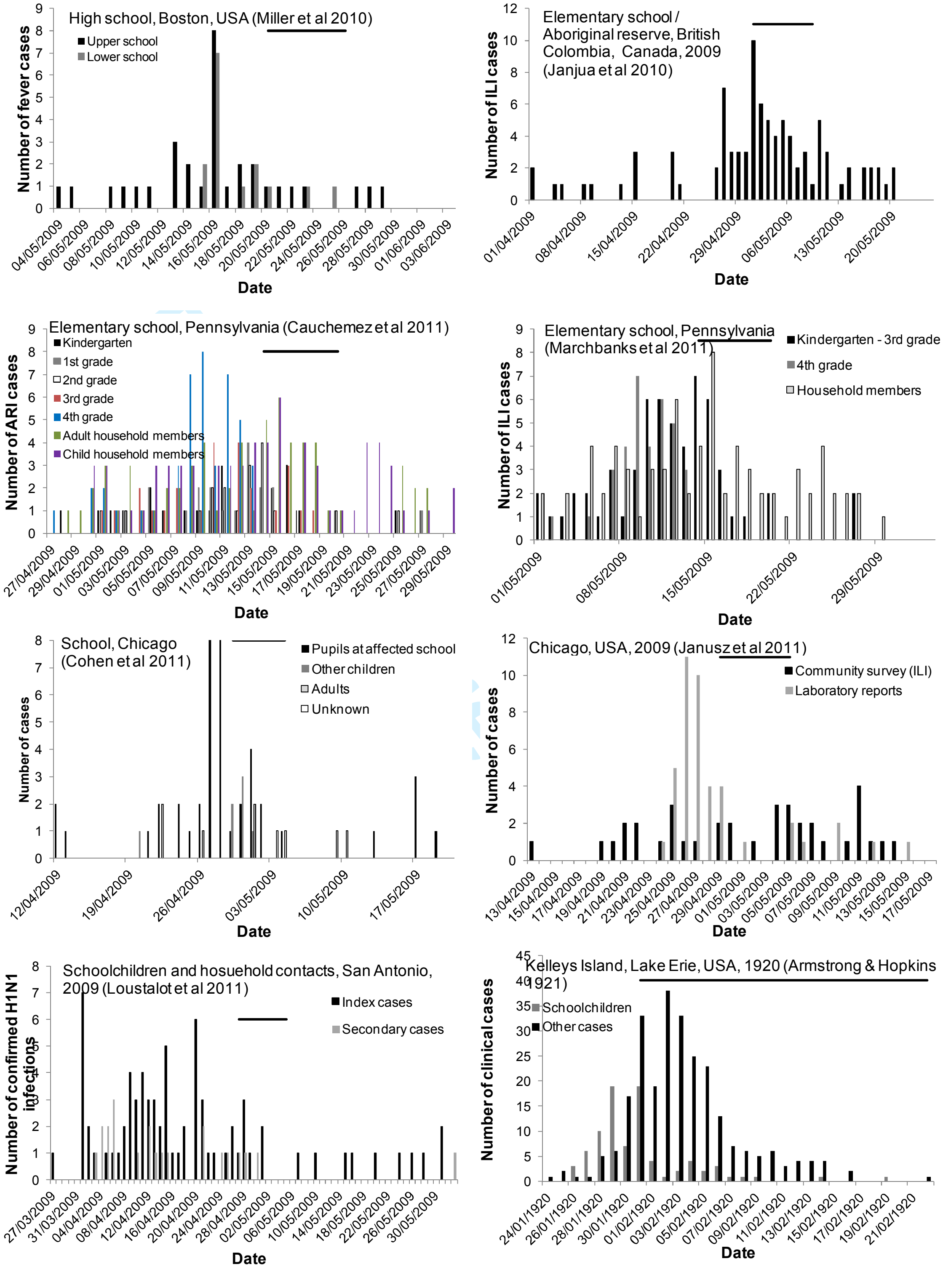


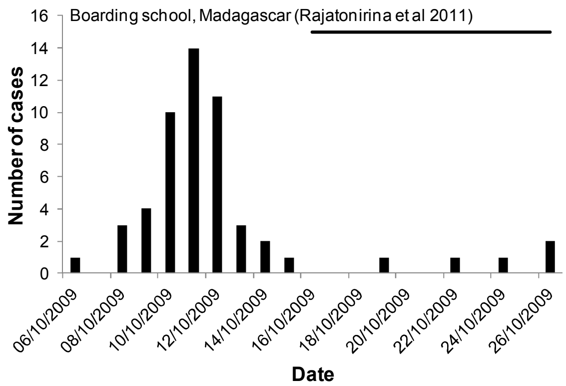
Secondary school, Toulouse, France (Guinard et al 2009)
Number of cases
Date
Includes both confirmed and probable cases
Paris, 2009 (Carrillo-Santisteve et al 2010)
Primary school
Nursery school
Families / friends
Number of cases
Date
Germany, 2009 (Poggensee et al 2010)
Practice index
Percentage of population with school holidays
Percentage of population living in states with school holidays
Week beginning
See Supplementary Information for definition of practice index
Vojvodina, Serbia 2009/10 (Petrovic et al 2011)
0-4 year olds
5-14 year olds
15-64 year olds
≥65 year olds
ILI consultation rate (per 100,000)
Week beginning
University and attached schools, Japan, 2009/10 (Uchida et al 2011)
Schoolchildren
University students
University staff
Number of cases
Week number (2009/10)
Japan (indigenously acquired cases only) (Nishiura et al 2009)
Number of confirmed cases
Date
Japan (Shimada et al 2009)
Number of confirmed cases
Date
Osaka, Japan (Kawaguchi et al 2009)
Number of confirmed cases
Date


Bangkok, 2009
(Chieochansin et al 2009)
All schools were closed for a public holiday 4-9/7/09 and in response to the outbreak 15-19/7/09. Tutorial schools were closed 13-28/7/09
Number of laboratroy confirmed H1N1 cases
Week beginning
Taipei City, Taiwan, 2009 (Hsueh et al 2010)
Hospitalisations
Class suspensions
Number of hospitalisations
Number of class suspensions
Week beginning
Primary school, Dongguan City, China, 2009 (Huai et al 2010)
Number of cases
Date
School, Hong Kong, 2009 (Leung et al 2011)
Schoolchildren
Household contacts
Number of confirmed H1N1 infections
Date
Israel, 2009 (Engelhard et al 2011)
<2 year olds
2-4 year olds
5-18 year olds
ILI consultation rate (per 10,000)
Week number (2009/10)
New Zealand, 2009 (Baker et al 2009)
ILI consultation rate (per 100,000 registered population)
Week ending
Three schools, Perth, Australia (Effler et al 2010)
One school closed completely, one cancelled classes for one grade, and one cancelled classes for three grades
Number of ILI cases
Date
Mexico (Echevarria-Zuno et al 2009)
Reporting requirements and case definition changed over the course of the outbreak. Schools closed in Mexico City and the State of Mexico on 24 April and nationally on 27 April. High schools reopened on 7 May and elementary schools on 11 May.
Some dates are taken from Stern & Markel 2009 or Cruz-Pacheco 2009.
Number of reported ILI cases
Date

6


Mexico, 2009 (Lajous et al 2010)
All cases
Severe cases
Number of ILI cases
Date
Mexico, 2009 (Chowell et al 2011a)
Students (5-20 years old)
Other age groups
Confirmed H1N1 infections
Week beginning
Peru, 2009 (Chowell et al 2011b)
Students (5-20 years old)
Other age groups
Confirmed H1N1 infections
Week beginning
Peru (Gomez et al 2009)
Number of SARI cases positive for H1N1
Week ending
Lima and Callao, 2009 (Gomez et al 2009)
5-9 year olds
10-19 year olds
20-59 year olds
Number of pneumonia cases
Week ending
Lima, Peru, 2009 (Tinoco et al 2009)
ILI
H1N1
Number of cases
Schools closed on 15 July
Week beginning
Lima, Peru, 2009 (Tinoco et al 2009)
<5 years
5-9 years
10-17 years
18-29 years
30-49 years
50-59 years
H1N1 rate per 1000
Schools closed on 15 July
Week beginning
High school, New York City, USA (Lessler et al 2009)
Number of ILI cases
Date


High school, Boston, USA (Miller et al 2010)
Upper school
Lower school
Number of fever cases
Date
Elementary school / Aboriginal reserve, British Colombia, Canada, 2009 (Janjua et al 2010)
Number of ILI cases
Date
Elementary school, Pennsylvania (Cauchemez et al 2011)
Kindergarten
1st grade
2nd grade
3rd grade
4th grade
Adult household members
Child household members
Number of ARI cases
Date
Elementary school, Pennsylvania (Marchbanks et al 2011)
Kindergarten - 3rd grade
4th grade
Household members
Number of ILI cases
Date
School, Chicago (Cohen et al 2011)
Pupils at affected school
Other children
Adults
Unknown
Number of cases
Date
Chicago, USA, 2009 (Janusz et al 2011)
Community survey (ILI)
Laboratory reports
Number of cases
Date
Schoolchildren and hosuehold contacts, San Antonio, 2009 (Loustalot et al 2011)
Index cases
Secondary cases
Number of confirmed H1N1 infections
Date
Kelleys Island, Lake Erie, USA, 1920 (Armstrong & Hopkins 1921)
Schoolchildren
Other cases
Number of clinical cases
Date


Boarding school, Madagascar (Rajatonirina et al 2011)
Number of cases
16
14
12
10
8
6
4
2
0
06/10/2009
08/10/2009
10/10/2009
12/10/2009
14/10/2009
16/10/2009
18/10/2009
20/10/2009
22/10/2009
24/10/2009
26/10/2009
Date

## Supplementary Table 1: Studies of the effects of school closures on seasonal influenza outbreaks

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| **Europe** | | | | | | | |
| Briscoe (1977) [1] | Outbreak report / estimate of vaccine efficacy | 1231 boys at Eton College, 1976 (79% of whom were vaccinated). Age of pupils not stated but the school currently takes boys aged 13-18. | Planned half term holiday | Friday 20 to Monday 23 February | Epidemic began in late January, first wave peaked 6 February, second wave peaked 17 February. | Clinical influenza (n = 372); confirmed as influenza A in 6/8 swabbed cases and influenza B in 1/8. | One case on day before break, ~12 cases on following day. ~1-4 cases/day for rest of study period. Hypothesised that closure curtailed the epidemics in individual school houses. 15/26 houses had no further cases after the break. |
| Davies et al (1988) [2] | Non-controlled intervention study of prophylactic amantadine | 859 boys aged 11-18 years at Christ's Hospital boarding school, 1986 | Planned half term holiday | Friday 21 to Monday 24 February | Epidemic began in early February, prophylaxis began on 5 February coinciding with the peak | Clinical influenza (n = 181); confirmed as influenza A H3N2 in majority of cases | 0-3 cases/day in five days preceding closure; 12 cases over 4-day closure period. Daily case numbers immediately following re-opening similar to those before closure. |
| Grilli et al (1989) [3] | Outbreak report | 675 boys aged 11-18 years at Christ's Hospital boarding school, 1985 | Planned mid-term break | 22-24 February | Epidemic began in late January and appeared to peak (at ~19 cases) 4 days before closure | ILI in pupils reporting to school infirmary (n = 206), the majority of which were confirmed as influenza. | 4-5 cases on each of the 2 days before closure; 15 cases occurred during closure (no daily breakdown is provided). ~0-6 cases occurred per day over the month following reopening. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Danis et al (2004) [4] | Outbreak report | 802 pupils at boys' secondary school (age 11-18 years), Ireland, 2003 | Response to outbreak | Whole school closed 4-11 September; 6th class sent home earlier (date not stated) | Whole school closure from day after peak of outbreak | ILI in absentees ascertained through telephone and questionnaire surveys (n = 107); confirmed as influenza in 12/15 cases | Peak incidence ~45 cases on day before closure; 18 cases on first day of closure and continuing decline thereafter. Only 2 cases after re-opening (although there was no active case finding at this point). Little evidence of community spread after the school outbreak. |
| Miller and Lee (1969) [5] | Outbreak report | England and Scotland (all ages), November 1967 – February 1968 | Planned Christmas holiday | Two weeks, all schools | Schools closed during the growth phase of the epidemic in most age groups | Age-specific rates of influenza reported by general practitioners | Rates in 0-4, 15-44, 45-64 and ≥65 year olds peaked during the second week of closure, rates in 5-14 year olds were in decline at this point. Following reopening, increases occurred in the 0-4 and especially 5-14 year age groups. |
| Cauchemez et al (2008) [6] | Statistical / transmission modelling analysis based on fitting to surveillance data | French national sentinel surveillance system, 1985-2006 (covering all ages, over 60 epidemic periods and from ~1% of practicing GPs) | Routine school holidays | Approx 2 weeks in each of December – January, February – March, March-April. Timing varies by 1-2 weeks in the 2-3 holiday zones. | Varied between epidemics | Rates of influenza-like illness reported through sentinel GPs | Estimated that holidays resulted in a 20-29% (median 24%) decrease in rate of transmission to children, without affecting contacts made by adults; this translated to a reduction in the attack rate of 16-18% overall (14-17% for adults, 18-21% for children) |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| **Asia** | | | | | | | |
| Olson et al (1980) [7] | Outbreak report | Grades 1-6 (2831 students) of Girls Teachers' Colleges Primary School, Taipei and grades 1-6 (650 students) of Taipei American School , Taiwan, September 1975 – May 1976. Ages of students not stated. | Planned holiday during virologically confirmed community influenza outbreak | Six weeks (Girls Teachers' Colleges Primary School); 3 weeks (Taipei American School) | Relationship with influenza circulation unclear, but likely to be late in the outbreak. Absenteeism at Girls Teachers' Colleges Primary School peaked two weeks before closure; absenteeism at Taipei American School had not exceeded the epidemic threshold at the time of closure. | School absenteeism (all cause) | Girls Teachers' Colleges Primary School: absenteeism declined from ~1.65 absences per child-day in the week before closure to ~0.7 absences per child-day (only slightly above expected absenteeism of 0.65) in the week following re-opening. Taipei American School: absenteeism very similar before and after closure |
| Sonoguchi et al (1985) [8] | Cohort study of the extent of cross-protection between influenza subtypes | 173 children (of 245 enrolled) aged 13-14 at a middle school in Tokyo; 347 children (of 374 enrolled) at a high school in Kumamoto prefecture, Japan. >90% vaccination coverage at each school. | Planned winter holiday (middle school); response to high levels of absenteeism (high school) | Two weeks (middle school); 3 days (high school) | Middle school: case numbers were fairly constant at <5/day during the week before closure. High school: epidemic appeared to be in decline when school closed but case numbers increased on reopening. | Absenteeism while the schools were open; serious, confirmed influenza A infection during closure periods. | Middle school: case numbers remained low at 0-2 per day during closure. High school: case numbers declined from 16 on the day before closure to 13, 5 and 0 on the three days of closure, rebounding to 21 on the day of reopening. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Fujii et al (2002) [9] | Presentation of surveillance data | Children aged 4-14 years attending 36 sentinel surveillance in Japan, 1999-2000 | Planned holiday | 2 weeks | Case numbers began to increase from week 50 of 1999; schools closed week 52 and week 1. | Medically attended clinical ILI | 191 cases in week before closure, declining by 38% to 118 cases during the first week of closure. Incidence increased to 173 cases during the second week of closure and an epidemic followed when schools reopened. |
| Heymann et al (2004) [10] | Ecological before-and-after comparison | All 6-12 year old children (n = 186094) registered with one of the four national healthcare insurance schemes, Israel, 2000 | National teachers' strike affecting ~80% of 6-12 year old children [11] coinciding with influenza outbreak | 2 weeks (16-28 January 2000), elementary schools nationwide. Ultra-orthodox schools, preschools and high schools remained open. | Outbreak began in last week of December 1999; schools closed 16-28 January 2000. | Medically attended / diagnosed respiratory tract infections (MARI); All physician visits; All outpatient clinic visits; All emergency department visits; hospitalisations; medication purchases (antibiotics, antipyretics, cold and cough medicines). | MARI: number of cases decreased by 42% and 27% during closure period and following fortnight respectively, compared to the fortnight before the closure.* Physician visits: rate ratios 0.78 and 0.88* No effect on hospital admissions. |
| Lo et al (2005) [12] | Ecological before-and-after comparison | Respiratory specimens (all ages) processed by Government Virus Unit, Hong Kong, 1998-2003 | Reaction to SARS outbreaks; other social distancing and hygiene measure also implemented | Not stated, but general community control measures were in effect at least in April – June 2003 | Not clear | Proportion of respiratory specimens positive for influenza | Monthly proportions positive were 58-88% lower in April – June 2003 than the average for the corresponding months of 1998-2003, but the difference with specific years was variable (e.g. little difference with the low influenza years of 1999 and 2000). |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Cowling et al (2008) [13] | Ecological before-and-after comparison with modelling analysis | Hong Kong population (all ages), 2008 | Reactive closure for 1 week in response to 3 influenza deaths in children, followed by scheduled 1 week Easter break. | 2 weeks (including Easter break) – all primary schools, special schools, kindergartens and day nurseries. | Outbreak began in January and peaked in February; schools closed 13 March. | Influenza A and B isolations from surveillance data as proportion of all specimens (for children and adults separately); sentinel ILI consultation rates; influenza hospital admission rates in children aged <5 years; estimates of effective reproduction number. | Continued decrease in already declining incidence measures; no apparent meaningful change in effective reproduction number. |
| Heymann et al (2009) [11] | Ecological before-and-after comparison, with comparison to years not affected by atypical school closure | Individuals aged ≥6 years registered with a specific healthcare service provider in Israel, 1998-2002 | Teachers' strike affecting ~80% of children, coinciding with influenza outbreak in 2000; Hanukah holidays in all years. | 8 days each year for Hanukah holiday; 2 week closure (16-28 January 2000) of elementary schools nationwide, excluding ultra-orthodox, preschools and high schools. | Closure due to strike as Heymann (2004) [10]; timing of Hanukah holidays in relation to respective epidemics not clear. | Ratio of number of clinic visits for ILI to number for non-respiratory illness, in 6-12 year olds and individuals aged over 12 (calculated separately for those living with and without 6-12 year olds). | Decrease in ratio of 15% for 6-12 year olds associated with the strike; decreases in adults were not statistically significant. In some years, there was evidence of a reduction in the ratio for adults and/or children associated with the Hanukah holidays. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| **Australasia** | | | | | | | |
| Cashman et al (2007) [14] | Outbreak report | Secondary boarding / day school (age of pupils not stated), New South Wales, Australia, August 2006 | Planned closure coinciding with outbreak of ILI and pneumonia | Four days | Unclear, but closure appears to have occurred late in outbreak | Presentations to sick bay with respiratory illness (n not stated). Influenza A H3N2 isolated from 5 students | Respiratory presentations decreased following closure, returning to baseline within 7 days (no further quantitative information provided). |
| Shaw et al (2006) [15] | Outbreak report | Single school in Wellington, New Zealand, May-June 2005 – 350 pupils in years 1-8. | One closure in response to high levels of absenteeism; later closure for a “holiday weekend” | Two closures of 4 days each, including weekends in both cases | Peak absenteeism occurred on the day before the first closure; epidemic was generally declining before the second closure | School absenteeism (all causes) | For both closures, absenteeism was lower on reopening than before the closure. |
| **Americas** | | | | | | | |
| Leonida (1970) [16] | Outbreak report | Five elementary schools (student population 2314) and three high schools (student population 8012) in Skokie, Illinois, September 1967 – April 1968 | Winter holiday | One week at the end of November and two weeks at the end of December; all schools in the sample | First closure 2 weeks before peak in elementary schools and 2 weeks after peak in high schools; second closure 2 weeks after peak in elementary schools and 6 weeks after peak in high schools. | School absenteeism due to ILI. | First closure had no clear effect on the increase in absenteeism at the elementary schools or the decline in the high schools. Absenteeism continued to decline in both elementary and high schools during the second closure; no apparent increase on reopening. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Glass et al (1978) [17] | Outbreak report | Mercer County, New Jersey, USA, November 1977 – March 1978 | Planned Christmas holiday | One week (public schools) or two weeks (residential schools) | Around peak of outbreak | Absenteeism from 6 public schools, work absenteeism, febrile illnesses in nursing homes, admissions to three residential school infirmaries, emergency room visits, hospital admissions for acute respiratory disease, P&I deaths, viral isolates | School absenteeism was lower after the holiday than before and gradually increased, reaching a plateau at a level slightly higher than before the closure. Emergency room visits and hospital admissions peaked during the closure week and viral isolates the week before. |
| Farley et al (1992) [18] | Outbreak report / estimate of vaccine efficacy | Boarding school, Connecticut (989 pupils in grades 9-12), January – April 1989 | Planned holiday | Three weeks | Epidemic appeared to be largely over by the time of the holiday (there were ~8 cases in the week before closure; the peak had occurred 5 weeks previously) | Admission to school infirmary with fever or respiratory symptoms ( n ~135) | Number of admissions remained low (≤8 per week) after reopening. |
| Louie et al (2007) [19] | Description of several surveillance systems during one influenza season | California, week 40 of 2005 to week 15 of 2006 | Planned winter holiday | Two weeks; presumably all schools | ILI peaked week before closure; laboratory isolations appeared to be increasing when schools were closed. | ILI reported through sentinel surveillance system (expressed as the proportion of all visits that were for ILI); number of laboratory-confirmed influenza from sentinel laboratories. | ILI declined throughout school closure and remained at low levels following reopening; laboratory-confirmed infections declined slightly in the first week of closure, then increased before declining after schools reopened. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Johnson et al (2008) [20] | Outbreak report focussing on effects of closure on families | 355 children enrolled in all 9 public elementary, middle and high schools in Yancey County, North Carolina, USA, 2006. | Closure for operational reasons, due to high levels of staff absenteeism largely attributed to ILI. | 10 days (2 – 12 November) - all 9 schools in the county. | First reported onset (in study sample) 20 October, epidemic peak 1 November, schools closed 2 November. | Parentally-reported ILI (n = 123) ascertained through telephone survey | Incidence decreased from peak of 8 cases the day before closure to 5 cases on the first day of closure, and continued to decline thereafter. |
| Rodriguez et al (2009) [21] | Cohort study comparing schools which cancelled their winter break to those which did not | 265 elementary, middle, high and “other” schools which closed and 205 which did not, King County, Washington, February – March 2007 | Planned holiday closure coinciding with influenza outbreak | 1 week, including middle, high and other public and private schools | Closure immediately following epidemic peak | School absenteeism (all causes) | No evidence of a difference in absenteeism following the break between schools that closed and those that did not. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Wheeler et al (2010) [22] | Ecological before-and-after comparison covering fortnights before, during and after school closure in 4 influenza seasons. | General population of Arizona, 2004/05 – 2007/08 influenza seasons. | Planned winter holidays | 2 weeks, all schools in the state | Peak occurred at least 2 weeks after reopening in 3 of the 4 seasons; peak coincided with the second week of closure in the remaining season. | Influenza laboratory reports 2004/05 to 2007/08 (n = 833 in school-aged children, 4036 in other age groups); influenza hospitalisations 2004/05 to 2006/07 (n = 885 in school-aged children, 4512 in other age groups). | For school-aged children, incidence never significantly increased during the two weeks of closure compared to the preceding two weeks; incidence in the two weeks following reopening either increased (2 seasons), declined (1 season) or was unchanged compared to the weeks of closure. For other age groups, incidence consistently increased during the closure period; changes on reopening were inconsistent. |

* Recalculated from data provided in paper

**Supplementary Table 2: Studies of the effects of school closures on pandemic influenza**

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| **Europe** | | | | | | | |
| Smith et al (2009) [23] | Outbreak report | 1307 pupils aged 13-18 at a boarding school in SE England, May – June 2009 | Scheduled break extended in response to outbreak; prophylactic oseltamivir also used | 11 days (4 day scheduled break extended by 7 days). Some pupils returned ~1 week earlier for exams | Closed around time of epidemic peak | Clinical ILI in pupils attending school healthcare facilities 1-27 May; laboratory-confirmed H1N1v after 27 May (n = 102 including both clinical and confirmed cases) | Apparent decline in cases in pupils following closure; no information on other age groups |
| HPA West Midlands H1N1v Investigation Team (2009) [24] | Outbreak report | 479 primary and nursery school pupils (aged 4-12), plus 84 staff, at a school in Birmingham, England, May 2009 | Scheduled break extended in response to outbreak; prophylactic oseltamivir also used | 11 days (9 day scheduled break extended by 2 days) | After epidemic peak | Laboratory confirmed H1N1v (n = 64) | Case numbers in pupils and staff declined following closure (e.g. from 8 cases on the day of closure to 5 on each of the two following days). No further cases following re-opening. Limited information on illness in other groups. |
| Wallensten et al (2009) [25] | Outbreak report | 248 Year 7 pupils at a school in SW England (93% of the year group, aged 11-12 years), April – May 2009 | Response to outbreak; prophylactic oseltamivir also used | 10 days | Unclear | Prevalence of self-reported ILI during the week before closure, the closure week, and the following week | 5, 11 and 10 children had symptoms compatible with the case definition in the week before, during and after closure, respectively. Absenteeism was almost identical in the weeks before and after closure. No information on illness in other age groups. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Calatayud et al (2010) [26] | Outbreak report | 1177 pupils (year groups Reception to 13), plus staff, at a school in London, May 2009 | Response to outbreak (preceded by closure for Easter several weeks previously); use of prophylactic oseltamivir | 3 days of Easter holiday remained after onset of first possible case; reactive closure lasted 9 days (including 2 weekends). | One possible case occurred 3 days before the end of the Easter closure and did not attend school while symptomatic; no further cases occurred until the main outbreak began ~7-10 days after this possible case. Reactive closure occurred the day following the peak (6 cases). | Virologically confirmed or possible (symptomatic without combined nose and throat swab but pending serological results) H1N1 infection | Cases continued to occur at 3-4 cases / day for 4 days following reactive closure. On the $5^{th}$ and $6^{th}$ days, there were 0 and 1 cases, respectively, and no cases subsequent to this. |
| Strong et al (2010) [27] | Outbreak report, focussing on use of antivirals | 297 pupils (aged 7-12 years) and 58 staff at a primary school in Sheffield, June 2009 | Response to outbreak; oseltamivir used for treatment and prophylaxis | One week | Epidemic peaked 3 days before closure. | Self-reported ILI (n = 61) | Incidence continued to decline while school was closed; no data presented for period after reopening. |
| Baguelin et al (2010) [28] | Modelling study of cost-effectiveness of vaccination; includes incidence data spanning term time and holiday periods. | England & Wales population, June – October 2009. | Planned summer holiday. | ~ 6 weeks, all schools nationally. | Closure coincided with peak of the first wave. | Health Protection Agency estimates of numbers of infections, rescaled (multiplied by 10) to reflect under-reporting. | Incidence declined throughout the period of school closure and increased after schools reopened, producing a second wave of infection. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Guinard et al (2009) [29] | Outbreak report | 30 students (aged 11-12 years) and 18 staff from one affected class, at a secondary school in Toulouse, France, June 2009 | Reactive closure in response to outbreak; some use of prophylactic oseltamivir | 7 days | At apparent end of epidemic | Probable H1N1v infection with or without laboratory confirmation (n = 17 with known date of onset, plus 3 without) | No further cases in pupils or their contacts following closure, but epidemic appeared to be over before the school was closed. |
| Carrillo-Santisteve et al (2010) [30] | Outbreak report | Two primary schools (360 and 293 aged 6-11 years), a nursery school (253 children aged 3-6 years) and a daycare school (unknown number of children aged 3 months to 3 years), Paris, June 2009; the four schools shared some facilities. | Response to outbreak which began in one of the primary schools; close contacts were given prophylactic oseltamivir. | 9 days (including 2 weekends), one of the primary schools and the nursery school (these schools accounted for 59/66 cases in pupils) | Officially closed on day of peak, but weekend began two days previously. | Confirmed and probable influenza cases in children attending the closed schools and their families and friends who consulted influenza outpatient clinic (n = 81) | Incidence in the closed primary school peaked on the 3rd day of closure (12 cases) and fell to 2 cases on each of the two following days; no further cases occurred. Incidence in the closed nursery school increased through the first 3 days of closure to a peak of 6 cases, then declined to 0-1 cases per day for 4 days; no further cases occurred after this. Cases in families and friends of the schoolchildren (n = 15) occurred only during the period of school closures. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Poggensee et al (2010) [31] | Outbreak report | General population of Germany, April – November 2009 | Planned holiday. | Duration not stated; school closure is described using the weekly "vacation density" (the percentage of the population living in states in which schools were closed) as the timing of the holiday varied between states | Vacation density peaked in the early stages of the outbreak, while the practice index was below the seasonal threshold and not increasing markedly. A second increase in the vacation density occurred while the practice index was increasing linearly. | Acute respiratory illness reported through sentinel surveillance system, used to calculate a "practice index" (defined as "the relative deviation of observed consultations for ARI divided by all consultations in the same week and set into relation to the background value of this ratio in weeks without influenza virus circulation") | Practice index remained fairly constant throughout the main school holiday period and increased only when the vacation density was declining; the second increase in the vacation density was followed by a brief plateau in the practice index. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Birrell et al (2011) [32] | Modelling analysis | General population of London, UK, May – December 2009 | Planned holidays | Six week summer holiday and two half terms of one week each (in May and October); all schools in London closed. | As Baguelin et al [28] (closure coincided with peak of the first wave) | Influenza-like illness recorded through GP sentinel surveillance scheme together with serological and virological data; parameters estimated included the reduction in contact rates associated with school holidays. | Both peaks in the two waves of consultations coincided with a school holiday. The summer holiday was estimated to reduce contacts amongst 5-14 year olds by 72% and the half term holiday by 48%; no effects were apparent in other age groups. |
| Evans et al (2011) [33] | Estimation of numbers of ILI cases due to pandemic H1N1 based on GP consultation data, helpline usage, virological swabbing and assumptions about the proportion of infections resulting in healthcare seeking. | General population of England, June – December 2009. | Planned holiday. | Six week summer holiday affecting all schools nationally. | As Baguelin et al [28] (closure coincided with peak of the first wave) | Estimate numbers of ILI cases due to pandemic H1N1, by age and region. | Estimated incidence declined during the school holiday and increased following reopening, in all regions and in all age groups except for the <1 and ≥65 year olds (among whom estimated case numbers were low). |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Smith et al (2011) [34] | Analysis of telephone helpline (NHS Direct) and GP consultation data | General UK population, May – August 2009; results also presented separately for London and West Midlands regions. | Planned school summer holiday (late July to early September). | Approximately six weeks; all schools nationally. | First week of school closure coincided with national peak in NHS Direct calls but occurred after the peak for London and the West Midlands. Consultation data peaked in the first week of closure nationally and before closure in London. | Weekly percentage of calls to NHS Direct that were classified as cold / flu.<br>Weekly GP consultation rates for ILI. | Both indices continued to decline during closure; no data presented after schools reopened. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Flasche et al (2011) [35] | Statistical analysis of relationship between estimated effective reproduction number for H1N1 pandemic influenza in 12 European countries (in 2009) and several explanatory variables, including school holiday dates | General populations in Belgium, Bulgaria, England, France, Germany, Italy, Luxembourg, Netherlands, Portugal, Romania, Slovakia and Spain, April – October 2009. School holidays occurred during the study period in all countries except Bulgaria, England and France. | Planned holidays. | Varied by country. | Varied by country, but typically early in the respective outbreaks. | Effective reproduction number estimated from numbers of laboratory-confirmed pandemic H1N1 infections. | No evidence found of a relationship between the effective reproduction number and the start of school holidays. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| van Gageldonk-Lafeber et al (2011) [36] | Outbreak report; comparison of pandemic and seasonal ILI consultation data. | General population of the Netherlands, and residents of nursing homes considered separately, October – December 2009 | Planned holidays | One week; all schools nationally although timing varied by region. | In north and central regions, schools closed two weeks after the epidemic threshold consultation rate was exceeded nationally; in the south, schools closed one week later. | GP consultation rates for ILI (age-stratified); ILI rates in nursing home residents; age-specific H1N1 hospital admission rates. | Possible reduction in incidence, or slowing of epidemic growth, among 0-4, 5-9, 10-14 and 15-19 year olds; epidemic continued to grow after schools reopened. No apparent effect of school closure on ILI in nursing home residents or hospital admissions. |
| Merler et al (2011) [37] | Modelling analysis of factors influencing spatiotemporal spread of pandemic H1N1 in Europe | General population of 37 European countries, May – December 2009 | Mainly planned holidays; some reactive closures. | Varied by country; summer holidays typically lasted 6-12 weeks and autumn holidays approximately 2 days to 2 weeks. | Varied by country. | Predicted numbers of infections for comparison with ILI surveillance data. | The model reproduced the observed incidence patterns in the different countries most closely when country-specific school holidays were included and contact rates in the population were allowed to change during holidays. (Transmission was assumed to be eliminated in schools and increased by a factor of 1.4 in the community during holidays.) |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Petrovic et al (2011) [38] | Outbreak report / analysis of risk factors for death in hospitalised cases. | Catchment population (n = 102,723) of general practices participating in sentinel surveillance, Vojvodina, Serbia, September 2009 – April 2010. | Response to outbreak. | All schools in Vojvodina; a closure lasting one week was followed six weeks later by a three week closure. | First closure coincided with first peak in ILI consultations in all ages and 5-14 year olds, but after the peak in 0-4 year olds. Second closure occurred after peak. | ILI consultation rates, overall and by age group. | ILI consultation rates declined following first closure and increased after schools reopened, particularly in 5-14 and 15-64 year olds. Rates were already declining when schools closed for second time and continued to do so during closure; possible slight increase after reopening. |
| **Asia** | | | | | | | |
| WHO (2009) [39] | Outbreak report, primarily reporting clinical aspects of infection | School pupils in Hyogo Prefecture and Osaka Prefecture, Japan, May 2009 | Response to school-associated outbreak | 7 days, >1400 schools closed but unclear whether this represents all schools in the two prefectures | Unclear | School absenteeism | No increase in school absenteeism upon reopening of schools (no quantification of absence levels given) |
| Nishiura et al (2009) [40], Shimada et al (2009) [41] | Outbreak reports (both report essentially the same data with slightly different analyses) | General Japanese population, May – June 2009 | Response to outbreak associated primarily with schools; some use of prophylactic oseltamivir [39] | 7 days (possibly more in some cases), all schools in Hyogo and Osaka prefectures (preceded by weekend closure) | First confirmed cases had disease onset on 9 May, weekend / closure began 16 May | Laboratory-confirmed H1N1 influenza (restricted to indigenously-acquired cases in [40] (n = 361[40] or 392 [41]) | Case numbers peaked at ~70 cases on the second day of the weekend, then declined throughout week of closure; no obvious resurgence on reopening |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Kawaguchi et al (2009) [42] | Outbreak report (subset of the data used in the two studies above) | Schools in Osaka Prefecture, Japan, May 2009; ages of affected students not stated. | Response to outbreak; some use of prophylactic oseltamivir in families of cases | 1 week (preceded by a weekend), all 270 high schools and 526 junior high schools, and most nurseries, primary schools, colleges and universities, in Osaka prefecture | Epidemic peaked on second day of closure (i.e. at the weekend) | Confirmed H1N1 infection (n = 156) | Peak of 30 cases on second day of weekend and declined throughout closure period; no resurgence after re-opening |
| Chieochansin et al (2009) [43] | Outbreak report | General population of Bangkok, June – July 2009 | Public holiday followed later by closure in response to outbreak | Public holiday lasted 1 week; schools were subsequently closed for 1 week and tutorial schools for 2 weeks | Public holiday occurred during peak week. Closure of schools and tutorial schools began during the following week. | Laboratory confirmed pandemic H1N1 influenza | Incidence declined throughout period of closure. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Wu et al (2010) [44] | Age-structured SIR model fitted to data on laboratory-confirmed cases during the 2009 pandemic in Hong Kong, used to estimate reporting rates and the reduction in within age group transmission resulting from school closures | General population of Hong Kong, June – August 2009 | Response to outbreak, followed by planned school holiday | All primary schools, kindergartens, childcare centres and special schools closed for ~1 month immediately prior to the summer holiday (duration of holiday not stated). Secondary schools with ≥1 case closed for 14 days, all secondary schools closed for summer holiday at same time as primary schools | At start of growth phase of first wave, which peaked around the 10th day of closure. School holidays started at the beginning of the growth phase of a second wave. | Laboratory-confirmed pandemic influenza cases, proportion of these in different age groups (0-12 years, 13-17 years and ≥18 years) and percentage reduction in within age group transmission resulting from school closures. | First wave continued to grow during school closure, followed by second wave beginning around the start of the school holidays. Following school closure, numbers of cases in 0-12 year olds remained low but the proportion of cases in this age group increased slightly, while that in 13-17 year olds decreased. School closure was estimated to reduce transmission between children of the relevant age group by 70% (95% CI 64-75%), corresponding to an overall reduction in transmission of ~25%. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Cowling et al (2010) [45] | Modelling analysis | General population of Hong Kong, May – October 2009 | Response to outbreak, followed by planned school holiday | All primary schools, kindergartens, childcare centres and special schools closed for ~1 month immediately prior to the summer holiday (duration of holiday not stated). Secondary schools with ≥1 case closed for 14 days, all secondary schools closed for summer holiday at same time as primary schools | At start of growth phase of first wave, which peaked around the 10th day of closure. School holidays started at the beginning of the growth phase of a second wave. | Laboratory-confirmed pandemic influenza cases and hospitalisations, used to estimate daily values of the effective reproduction number. | Effective reproduction number declined during initial days of closure, oscillated around 1 for the duration of the closure period, increased very slightly when schools reopened before declining again. |
| Hsueh et al (2010) [46] | Outbreak report | General population of Taipei City, Taiwan, June 2009 – January 2010 | Response to outbreak | Individual classes suspended for at least 5 days if >2 students had confirmed infection within 3 days. | Timing for individual schools not presented; number of class suspensions generally increased with the number of hospitalisations. | Hospitalisations with pandemic H1N1. | Number of class suspensions generally followed the number of hospitalisations. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Wu et al (2010) [47] | Vaccine study amongst children attending public primary and middle schools and participating in a national celebration parade. | 95244 vaccinated participants in a national celebration parade, Beijing; of these, 25037 vaccinated schoolchildren were compared to 244091 unvaccinated schoolchildren. | Planned national holiday | 1 week, all schools nationally. | Schools closed as cumulative incidence in unvaccinated students began to plateau | Laboratory confirmed H1N1 infection | Cumulative incidence in unvaccinated children increased very slightly during the school closure (from ~220 to ~260 per 100,000); rate of increase in cumulative incidence increased ~1 week after schools reopened. Cumulative incidence in vaccinated students remained relatively constant before, during and after school closure. |
| Huai et al (2010) [48] | Outbreak report | Primary school (1314 pupils) in Dongguan City, Guangdong Province, China, June 2009 | Response to outbreak, shortly followed by planned summer break. | Affected primary school closed 19-28 June; all schools in the town closed 22-28 June, Planned summer break began on 2 July. | Affected school closed on day of peak. | Confirmed or suspected cases in children attending affected school (n = 105); limited data on cases in the community are also included. | Epidemic in schoolchildren peaked at 30 cases on the first day of closure, declining to 11 the following day. No further cases occurred between the last two days of closure and the subsequent closure for the holiday. |
| Engelhard et al (2011) [49] | Outbreak report | Children aged <18 years enrolled with one health maintenance organisation in Israel, June 2009 – April 2010. | Two separate planned holidays. | Summer holiday lasted 9 weeks, autumn holiday lasted 5 weeks. | Summer holiday occurred close to beginning of first wave; autumn holiday close to beginning of second. | Rate of ILI (fever with one or more of cough, coryza, sore throat, myalgia) visits to community health clinics. | ILI rate peaked and decliend during summer holiday, began to increase when schools reopened and reached a second peak during the autumn holiday before declining again. A third wave occurred after the autumn holiday. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Leung et al (2011) [50] | Outbreak report / analysis of household secondary attack rates and effect of oseltamivir. | 511 children attending a secondary school in Hong Kong and their 205 household contacts, June 2009. No cases occurred amongst the 153 school staff. | Response to outbreak | Two weeks, coinciding with closure of all schools in Hong Kong. | Three days after peak. | Laboratory-confirmed pandemic H1N1 in schoolchildren or household contacts. | Incidence increased during first two days of closure and subsequently remained very low; last case occurred one week before reopening. |
| Uchida et al (2011) [51] | Prospective study of pandemic H1N1 | 2318 schoolchildren, 11424 university students and 3344 staff members associated with Shinshu University Organisation, August 2009 – March 2010 | Planned breaks and reactive closures. | Planned summer holiday affected all schools for approximately one month; winter holiday for 3 weeks; reactive school and class closures varied for individual schools. | Summer holiday occurred before outbreak began; winter holiday occurred while incidence was declining. Timing of reactive closures in relation to incidence in individual schools unclear. | "Influenza-like symptoms and diagnosed with confirmed, probable or suspected swine flu at hospital or clinics." | Incidence continued to decline during the winter holiday. Incidence also appeared to declined during reactive school and class closures, but this is unclear as data are not presented for individual schools. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| **Africa** | | | | | | | |
| Rajatonirina et al (2011) [52] | Outbreak report / analysis of oseltamivir compliance and side effects. | 132 boarders at a school in Antananarivo, Madagascar, October – November 2009. | Planned holiday | 2 weeks | After main phase of epidemic. | At least one influenza-like symptom (n = 56 with known onset date). | Epidemic appeared to be largely over when the school closed; sporadic cases continued to occur during closure period. |
| **Australasia** | | | | | | | |
| Caley et al (2008) [53] | Transmission modelling analysis of hospitalisation and mortality data | Sydney, 1919 (all ages) | Response to outbreak; combined with other social distancing interventions | ~4.5 weeks initially; schools reopened for ~3 weeks and then closed for a further ~2 months. | Initial closure occurred as first cases were detected; second closure occurred during exponential growth phase of epidemic. | Estimated reduction in "behaviours resulting in disease transmission." | Transmission reduced by 38% during period of school closure. |
| Baker et al (2009) [54] | Outbreak report | New Zealand population, April – August 2009 (all ages) | Planned national holiday during national outbreak; some use of prophylactic antivirals during containment phase [55] | 2 weeks, apparently all schools nationally | Depending on indicator, closure coincided with peak, preceded it by 1 week, or followed it by 1-3 weeks | Cases reported through notifiable disease surveillance system (n = 3179); hospitalisations amongst these cases (n = 972); ICU influenza admissions (n = 106); GP consultation rates (two surveillance systems) | Notifications, hospitalisations and ICU admissions began to decline during second week of closure. GP consultation rates for 5-14 year olds increased following re-opening (in one of the systems only). |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Effler et al (2010) [56] | Outbreak report focussing on children's activities during closure and the effects of closure on families | Three schools in Perth, Western Australia, May – July 2009; ages of affected pupils not stated. Data available for 233 of 402 students. | Response to outbreak | 1 week; one school closed completely and two closed only affected year groups | Confirmed cases in individuals attending the three schools peaked two days before closure | Confirmed pandemic H1N1 infection | Confirmed cases peaked at ~9/day two days before closure, subsequently a maximum of 1 case / day occurred. |
| Paine et al (2010) [57] | Outbreak report and modelling analysis | New Zealand population, April – November 2009 (all ages) | Planned national holiday during national outbreak; some use of prophylactic antivirals during containment phase [55] | 2 weeks, all schools nationally | ~4 days before peak. | Cases reported through notifiable disease surveillance system (n = 3254), used to estimate daily values of the effective reproduction number | Case numbers peaked and declined during holiday, no consistent increase when schools reopened. Effective reproduction number was declining before school closure and continued to decrease during the holiday, appeared to increase slightly and reach a plateau after schools reopened. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| **Americas** | | | | | | | |
| Cruz-Pacheco et al (2009) [58] | Estimation of contact rates based on estimated values of $R_0$ before and after introduction of control measures | Mexico City, April – May 2009 (all ages) | Response to outbreak; no use of antivirals | ~2.5 weeks, all schools in Mexico City. | Epidemic had been growing exponentially for ~1 week when schools were closed | Number of confirmed (n = 1752) or probable (n = 6114) cases; estimated daily reproduction number ($R_t$) | Incidence increased initially to peak of ~400 probable and 150 confirmed cases/day on second and third days of closure, then declined gradually over the closure period. $R_t$ declined from ~1.6 before and during the closure, crossing 1 within 2 days of closure and remaining <1 thereafter. |
| Echevarria-Zuno et al (2009) [59] | Outbreak report | National population of Mexico, April – July 2009 | Response to outbreak; no mention of antiviral prophylaxis | Approx two weeks; entire education system (including nurseries and universities) initially in Mexico City and Mexico State from 23 April, then nationwide from 27 April [60]. Universities and high schools reopened 4-5 days before elementary schools [58]. | Schools closed early in growth phase of epidemic. | ILI reported through active surveillance of inpatients and outpatients | Epidemic continued while schools were closed and peaked ~1 week after closure; increase in cases over three days after reopening of universities and high schools, but not following subsequent reopening of elementary schools. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Lajous et al (2010) [61] | Outbreak report | 56,551 respondents to a text message survey, Mexico, April 2009 | Both planned closure and a response to the outbreak | Planned holiday lasted 1 week; reactive closure lasted at least one week (schools were still closed at the end of the time period presented) | Planned closure occurred in the early stages of the outbreak before national surveillance indicated an increase in the number of cases but case numbers from survey data were declining. Reactive closure occurred during the increase in national case numbers. | ILI in survey respondents; suspected or confirmed H1N1 from national surveillance | Planned closure was followed by a slight decrease in case numbers reported through national surveillance, but this increased before schools reopened. National surveillance data peaked ~3 days after the reactive school closure and then declined through the rest of the closure period. Survey data were not obviously affected by school closure, although the proportion of reported cases which prevented respondents working declined during both closure periods. |
| Gomez et al (2009) [62] | Outbreak report | National population of Peru, May – September 2009 | Appears to be reactive, but unclear; some use of prophylactic oseltamivir | 3 weeks, all schools nationwide | One week after peak week | Number of pneumonia cases in 5-59 year olds in Lima and Callao; number of severe acute respiratory infections nationally | Pneumonia cases decreased from peak week ~130 cases following closure to ~40 cases and showed slight resurgence to just below 60 cases when schools re-opened; effect on other severe respiratory infections difficult to assess as date of closure is unclear. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Tinoco et al (2009) [63] | Prospective cohort study | 1747 individuals in 343 randomly selected households, San Juan de Miraflores District, Lima, Peru, May – August 2009 | Unclear | ~3 weeks, presumably all schools | After peak | Influenza-like illness counts by causative organism (H1N1 or other); age-specific rates of confirmed H1N1v | Number of ILI cases (and confirmed H1N1) decreased throughout closure period, from 54 (39 H1N1) the preceding week to 29 (19), 12 (6) and 6 (3) in each subsequent week; rates of confirmed H1N1 reached zero in week following closure in all age groups except 50-59 year olds. |
| Lessler et al (2009) [64] | Outbreak report | 1453 students (aged 14-19) and staff at a New York City high school, April – May 2009 | Response to outbreak | 9 days, one school | After peak | Confirmed H1N1 influenza or self-reported ILI | Incidence already declining when school was closed, continued to decline through closure period. No data presented for period following re-opening. |
| Miller et al (2010) [65] | Survey of schoolchildren regarding behaviour during reactive school closure | Private girls' school in Boston, USA; 63 of 176 children in grades 5-8 and 188 of 240 in grades 9-12. | Response to outbreak / high levels of absenteeism | One week | 4 days after peak | Fever in pupils with ILI, and absenteeism, in upper and lower school separately | Upper and lower schools each had one case of fever on the first day of closure and continued to have 0 or 1 case per day throughout the closure period; no apparent increase on reopening. Absenteeism in both schools was considerably higher before closure than after reopening. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Janjua et al (2010) [66] | Telephone survey of households of children enrolled in any of the six schools in the community, primarily aimed at conducting a case-control study of the effect of vaccination against seasonal influenza on risk of infection with pandemic H1N1. | Elementary school and surrounding community, British Colombia, Canada, April – May 2009. | Response to outbreak in one elementary school | 9 days | Outbreak peaked on the first day of school closure | ILI (n = 92) in 1092 participants from households of children attending any school in the community | Daily number of cases declined during school closure (from 10 cases on the first day to 1 case on the final day), increasing to 5 cases on the day of reopening. Case numbers ranged from 0-3 per day for the remainder of the study period. |
| Marchbanks et al (2011) [67] | Outbreak report | 388 of 456 pupils at an elementary school in Pennsylvania, USA, and 957 household contacts, May 2009. | Response to outbreak | 7 days | ILI peaked two days before school closure. | ILI (93 pupils and 74 contacts): subjective fever with cough and / or sore throat. | Incidence increased on second day of closure and then declined; very slight increase on reopening (although absenteeism returned to normal). No cases occurredin the 4$^{th}$ grade during closure or after reopening. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Cauchemez et al (2011) [68] | More detailed modelling analysis of outbreak described in Marchbanks et al [67] | Same school as Marchbanks et al [67], but using data from 27 April to 30 May 2009 from 370 pupils and 899 household contacts. | As Marchbanks et al [67] | As Marchbanks et al [67] | ARI epidemic curve peaked 2 and 3 days before closure. | Acute respiratory infection (at least two of fever, cough, sore throat, runny nose) in children attending the affected school (stratified by grade) and their household contacts (stratified into adults and children).129 cases in pupils and 141 in household contacts. | Incidence increased on the second day of closure but then declined; slight increase on reopening. Statistical analysis found no evidence of an effect of closure on the transmission rate among pupils (30% reduction, 95% credible interval 62% decrease to 22% increase). Reproduction number was also similar (0.3) during the week of closure and the following week. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Janusz et al (2011) [69] | Outbreak report and community-based survey. Community survey collected data from 240 of 711 households approached (comprising 644 individuals). | A community associated with a school which experienced an outbreak, Chicago, USA, April – May 2009. | Response to outbreak. | 7 days; one of the five elementary schools in the community closed. | Approximately one third of ILI cases reported through the survey had occurred before school closure (0-3 per day). Only 4 laboratory-confirmed cases had been reported to the Department of Health before closure. | ILI (fever with cough and / or sore throat, n = 37) in the survey; laboratory confirmed H1N1 infection reported to Chicago Department of Public Health (n = 43) based on date of specimen collection, although the peak based on date of onset occurred 3 days before closure. | In the community survey, maximum of 3 cases per day before and during closure; no increase when school reopened. None of the cases reported through this survey were linked to the affected school.<br><br>Laboratory reports peaked on the first day of closure, generally declined during closure and remained low after reopening; however, testing recommendations changed on the second day of closure. |
| Cohen et al (2011) [70] | Outbreak report | Pupils at a school in Chicago which closed due to the outbreak, and their household contacts (170 households, of 609 eligible, provided data), April – May 2009. | Response to outbreak. | 1 week. | Highest numbers of cases were reported on the two days before closure. | Acute respiratory illness (one or more of fever, cough, sore throat, rhinorrhoea or nasal congestion, n = 58). | Case numbers were lower on the first day of closure than on the two previous days, increased during closure and then declined. Few cases were reported after school reopened. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Loustalot et al (2011) [71] | Questionnaire survey / assessment of household secondary attack rate and use of non-pharmaceutical interventions. | 668 households (2772 individuals) of 1716 approached, with children attending a closed high school in San Antonio, Texas, March – June 2009. | Response to outbreak | 9 days | Peak occurred 8 days before school closure | ILI in household members reported by one adult household member, stratified into index cases (students attending the affected school, n = 78) and secondary cases (n = 21) | Incidence remained low during closure; no cases reported on the final four days of closure. 1-2 cases per day after school reopened. |
| Chowell et al (2011a) [72] | Epidemiological and modelling analysis of outbreak data | 107 million individuals registered with a Mexican private medical system, April – December 2009 | Response to outbreak, and a later planned summer holiday. | Reactive closure lasted from 24 April to 5 May; summer holiday lasted ~7 weeks; all schools nationally were closed. | Reactive closure occurred early in the first wave of the outbreak (together with other interventions); summer holiday followed a plateau in the number of confirmed cases. | Confirmed pandemic H1N1 cases or ratio of number of cases in students (aged 5-20 years) to number of cases in other age groups. | Reactive closure appeared to slow epidemic growth, which resumed when interventions were lifted. Incidence was reasonably constant in all ages during the summer holiday but declined amongst students; cases amongst students and others increased when schools reopened (as did the ratio of student to non-student cases). |
| Herrera-Valdez et al (2011) [73] | Modelling analysis, including estimation of change in contact rate during school closure period. | National population of Mexico, April – November 2009 | One reactive closure and a subsequent planned holiday | Reactive closure lasted ~2 weeks; holiday lasted ~2 months. | Schools closed reactively early in growth phase; holiday started close to the peak of the second wave. | Confirmed pandemic H1N1 cases; model estimates of contact rate. | Confirmed cases occurred in three waves corresponding to closing and reopening of schools. Estimated contact rates appeared to be reduced by ~80% during school closure periods. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Chowell et al (2011b) [74] | Epidemiological / spatial analysis of outbreak data | General population of Peru, May – December 2009 | Planned school holiday moved forward by two weeks | Three weeks, all schools in the country | After the peak in daily national data; same week as peak in weekly data stratified into students and others. | Confirmed pandemic H1N1 cases or ratio of number of cases in students (aged 5-20 years) to number of cases in other age groups. | Number of cases in whole population, students and others declined throughout closure period; no clear increase on reopening. Ratio of student to non-student cases had already peaked, but declined during closure and increased afterwards. |
| Monto et al (1970) [75] | Non-randomised community trial of pandemic vaccine | All schoolchildren in Tecumseh (approx 3680) and Adrian (number not stated), Michigan, November 1968 – January 1969. 86% of children and a small number of adults in Tecumseh were vaccinated against the pandemic strain. Pandemic vaccine was not used in Adrian. | Christmas holiday | Two weeks, presumably all schools | Peak absenteeism in Adrian occurred one week before closure; Tecumseh did not experience an extensive epidemic. | School absenteeism (all causes) | Absenteeism in Adrian was >14% on each of the four days before closure and was ~8% on the day of reopening. Tecumseh did not experience any clear peaks in absenteeism. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Bootsma and Ferguson (2007) [76] | Statistical / transmission modelling analysis of historical P&I mortality data | 23 US cities with data on timing of introduction of NPIs during 1918 influenza pandemic | Response to outbreaks; other social distancing measures also implemented | Approx 0-7 weeks, depending on city | Varied by city | Excess total or peak mortality in each city | Correlation between excess / peak mortality and timing of introduction of NPIs relative to progress of epidemic ($p<0.01$ in both cases). Lifting of NPIs allowed transmission to become established again |
| Hatchett et al (2007) [77] | Statistical analysis of historical P&I mortality data | 17 US cities, September – December 1918 | Response to outbreaks; other social distancing measures also implemented | Varied by city | Varied by city | Cumulative Excess P&I death rates (CEPID) | Cities which closed schools before CEPID reached 30/100,000 had a lower median peak weekly excess P&I death rate than those which did not ($p<0.01$) but there was no significant difference in median CEPID.<br>Closing schools at a higher CEPID was associated with higher peak P&I death rates (Spearman $\rho$ =0.54) but not with total P&I death rates. Second waves occurred only after lifting of NPIs. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Markel et al (2007) [78] | Statistical analysis of historical mortality data | 43 US cities, September 1918 – February 1919 | Response to outbreaks; other social distancing measures also implemented | Varied by city | Varied by city | Weekly excess P&I death rates | Not uniform across cities (but this could be related to the timing of the intervention). Earlier interventions correlated with increased time to epidemic peak (r = -0.74, p<0.001), reduced peak excess death rate (r = 0.31, p=0.02) and reduced total excess death rate (r = 0.37, p=0.008). Increased duration of intervention associated with reduced total excess death rate (r = -0.39, p=0.005). |
| Jordan et al (1919) [79] | Outbreak report | Elementary school (391 pupils aged 4-13 years) and high school (427 pupils aged 14-18 years) of University of Chicago, October – December 1918 | Planned Thanksgiving break | Four days (including weekend) | Both schools were closed for final three days of peak week and one day of the following week. | Clinical influenza (n = 97 in elementary school, n = 91 in high school) | Elementary school: incidence declined from 19 cases in peak week to 15 the following week, showed a second peak of 10 cases 3 weeks after the closure. High school: incidence decreased from 16 cases in peak week to 5 the following week, showed a second peak of 11 cases 2 weeks after the closure. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Armstrong and Hopkins (1921) [80] | Outbreak report | Kelleys Island, Lake Erie, US, January – February 1920, population 689 (of whom 157 were schoolchildren) | Response to staff and student absenteeism during influenza outbreak | The single school (for both grammar and high school pupils) on the island remained closed "until the epidemic had subsided" | Epidemic began 24 January, school closed 30 January | Self-reported clinical influenza, based on checklist of symptoms ( n = 369) | Overall incidence peaked at 52 cases on day following closure. Cases in schoolchildren dipped on day of closure, peaked following day and declined thereafter. Cases in other groups dipped two days after closure, peaked the following day and then declined. |

**Supplementary references**

1. Briscoe JH. The protective effect of influenza vaccine in a mixed influenza A and B epidemic in a boys' boarding school. *J R Coll Gen Pract* 1977;27(166):28-31.
2. Davies JR, Grilli EA, Smith AJ, Hoskins TW. Prophylactic use of amantadine in a boarding school outbreak of influenza A. *J R Coll Gen Pract* 1988;38(313):346-8.
3. Grilli EA, Anderson MJ, Hoskins TW. Concurrent outbreaks of influenza and parvovirus B19 in a boys' boarding school. *Epidemiology and Infection* 1989;103(2):359-69.
4. Danis K, Fitzgerald M, Connell J, Conlon M, Murphy PG. Lessons from a pre-season influenza outbreak in a day school. *Commun Dis Public Health* 2004;7(3):179-83.
5. Miller DL, Lee JA. Influenza in Britain 1967-68. *J Hyg (Lond)* 1969;67:559-72.
6. Cauchemez S, Valleron A-J, Boelle P-Y, Flahault A, Ferguson NM. Estimating the impact of school closure on influenza transmission from Sentinel data. *Nature* 2008;452(7188):750-4.
7. Olson JG. School absenteeism during an outbread of B/Hong Kong/5/72-like influenze virus in Taipei, Taiwan. *Southeast Asian J Trop Med Public Health* 1980;11(4):429-34.
8. Sonoguchi T, Naito H, Hara M. Cross-subtype protection in humans during sequential, overlapping, and/or concurrent epidemics caused by H3N2 and H1N1 influenza viruses. *Journal of Infectious Diseases* 1985;151(1):81-88.
9. Fujii H, Takahashi H, Ohyama T, Hattori K, Suzuki S. Evaluation of the school health surveillance system for influenza, Tokyo, 1999-2000. *Japanese Journal of Infectious Diseases* 2002;55(3):97-98.
10. Heymann A, Chodick G, Reichman B, Kokia E, Laufer J. Influence of school closure on the incidence of viral respiratory diseases among children and on health care utilization. *Pediatr Infect Dis J* 2004;23(7):675-7.
11. Heymann AD, Hoch I, Valinsky L, Kokia E, Steinberg DM. School closure may be effective in reducing transmission of respiratory viruses in the community. *Epidemiol Infect* 2009;137(10):1369-76.
12. Lo JY, Tsang TH, Leung YH, Yeung EY, Wu T, Lim WW. Respiratory infections during SARS outbreak, Hong Kong, 2003. *Emerg Infect Dis* 2005;11(11):1738-41.
13. Cowling BJ, Lau EHY, Lam CLH, Cheng CKY, Kovar J, Chan KH, et al. Effects of school closures, 2008 winter influenza season, Hong Kong. *Emerg Infect Dis* 2008;14(10):1660-2.
14. Cashman P, Massey P, Durrheim D, Islam F, Merritt T, Eastwood K. Pneumonia cluster in a boarding school--implications for influenza control. *Commun Dis Intell* 2007;31(3):296-8.
15. Shaw C, McLean M, McKenzie J. Other surveillance reports: influenza-like illness in Wellington schools 2005. *New Zealand Public Health Surveillance Report* 2006;4(2):4-6.
16. Leonida DDJ. Morbidity patterns reflected in a school health program during an influenza epidemic season. *Illinois Medical Journal* 1970;137(3):262-64.
17. Glass RI, Brann EA, Slade JD, Jones WE, Scally MJ, Craven RB, et al. Community-wide surveillance of influenza after outbreaks due to H3N2 (A/Victoria/75 and A/Texas/77) and H1N1 (A/USSR/77) influenza viruses, Mercer County, New Jersey, 1978. *J Infect Dis* 1978;138(5):703-6.
18. Farley TA, St. Germain JM, Chamberlain LA, Krassner L. The impact of influenza vaccination on respiratory illness at a boarding School. *Journal of American College Health* 1992;41(3):127-31.

19. Louie JK, Schnurr DP, Guevara HF, Honarmand S, Cheung M, Cottam D, et al. Creating a Model Program for Influenza Surveillance in California. Results from the 2005-2006 Influenza Season. *American Journal of Preventive Medicine* 2007;33(4):353-57.
20. Johnson AJ, Moore ZS, Edelson PJ, Kinnane L, Davies M, Shay DK, et al. Household responses to school closure resulting from outbreak of influenza B, North Carolina. *Emerg Infect Dis* 2008;14(7):1024-30.
21. Rodriguez CV, Rietberg K, Baer A, Kwan-Gett T, Duchin J. Association between school closure and subsequent absenteeism during a seasonal influenza epidemic. *Epidemiology* 2009;20(6):787-92.
22. Wheeler CC, Erhart LM, Jehn ML. Effect of school closure on the incidence of influenza among school-age children in Arizona. *Public Health Rep* 2010;125(6):851-9.
23. Smith A, Coles S, Johnson S, Saldana L, Ihekweazu C, O'Moore E. An outbreak of influenza A(H1N1)v in a boarding school in South East England, May-June 2009. *Euro Surveill* 2009;14(27):9.
24. Health Protection Agency West Midlands H1N1v Investigation Team. Preliminary descriptive epidemiology of a large school outbreak of influenza A(H1N1)v in the West Midlands, United Kingdom, May 2009. *Euro Surveill* 2009;14(27).
25. Wallensten A, Oliver I, Lewis D, Harrison S. Compliance and side effects of prophylactic oseltamivir treatment in a school in South West England. *Euro Surveill* 2009;14(30):19285.
26. Calatayud L, Kurkela S, Neave PE, Brock A, Perkins S, Zuckerman M, et al. Pandemic (H1N1) 2009 virus outbreak in a school in London, April-May 2009: an observational study. *Epidemiol Infect* 2010;138(2):183-91.
27. Strong M, Burrows J, Stedman E, Redgrave P. Adverse drug effects following oseltamivir mass treatment and prophylaxis in a school outbreak of 2009 pandemic influenza A(H1N1) in June 2009, Sheffield, United Kingdom. *Euro Surveill* 2010;15(19):pii/19565.
28. Baguelin M, Hoek AJV, Jit M, Flasche S, White PJ, Edmunds WJ. Vaccination against pandemic influenza A/H1N1v in England: A real-time economic evaluation. *Vaccine* 2010;28(12):2370-84.
29. Guinard A, Grout L, Durand C, Schwoebel V. Outbreak of influenza A(H1N1)v without travel history in a school in the Toulouse district, France, June 2009. *Euro Surveill* 2009;14(27).
30. Carrillo-Santisteve P, Renard-Dubois S, Cheron G, Csaszar-Goutchkoff M, Lecuit M, Lortholary O, et al. 2009 pandemic influenza A(H1N1) outbreak in a complex of schools in Paris, France, June 2009. *Euro Surveill* 2010;15(25):24.
31. Poggensee G, Gilsdorf A, Buda S, Eckmanns T, Claus H, Altmann D, et al. The first wave of pandemic influenza (H1N1) 2009 in Germany: From initiation to acceleration. *BMC Infectious Diseases* 2010;10(155).
32. Birrell PJ, Ketsetzis G, Gay NJ, Cooper BS, Presanis AM, Harris RJ, et al. Bayesian modeling to unmask and predict influenza A/H1N1pdm dynamics in London. *Proceedings of the National Academy of Sciences of the United States of America* 2011;108(45):18238-43.
33. Evans B, Charlett A, Powers C, McLean E, Zhao H, Bermingham A, et al. Has estimation of numbers of cases of pandemic influenza H1N1 in England in 2009 provided a useful measure of the occurrence of disease? *Influenza and other Respiratory Viruses* 2011;5(6):e504-e12.
34. Smith S, Smith GE, Olowokure B, Ibbotson S, Foord D, Maguire H, et al. Early spread of the 2009 infuenza A(H1N1) pandemic in the United Kingdom - use of local syndromic data, May-August 2009. *Eurosurveillance* 2011;16(3).

35. Flasche S, Hens N, Boelle P-Y, Mossong J, van Ballegooijen WM, Nunes B, et al. Different transmission patterns in the early stages of the influenza A(H1N1)v pandemic: a comparative analysis of 12 European countries. *Epidemics* 2011;3(2):125-33.
36. Van Gageldonk-Lafeber AB, Hooiveld M, Meijer A, Donker GA, Veldman-Ariesen MJ, van der Hoek W, et al. The relative clinical impact of 2009 pandemic influenza A (H1N1) in the community compared to seasonal influenza in the Netherlands was most marked among 5-14year olds. *Influenza and other Respiratory Viruses* 2011;5(6):e513-e20.
37. Merler S, Ajelli M, Pugliese A, Ferguson NM. Determinants of the spatiotemporal dynamics of the 2009 H1N1 pandemic in europe: Implications for real-time modelling. *PLoS Computational Biology* 2011;7(9).
38. Petrovic V, Seguljev Z, Cosic G, Ristic M, Nedeljkovic J, Dragnic N, et al. Overview of the winter wave of 2009 pandemic influenza A(H1N1)v in Vojvodina, Serbia. *Croatian Medical Journal* 2011;52(2):141-50.
39. Human infection with new influenza A (H1N1) virus: clinical observations from a school-associated outbreak in Kobe, Japan, May 2009. *Wkly Epidemiol Rec* 2009;84(24):237-44.
40. Nishiura H, Castillo-Chavez C, Safan M, Chowell G. Transmission potential of the new influenza A(H1N1) virus and its age-specificity in Japan. *Euro Surveill* 2009;14(22):4.
41. Shimada T, Gu Y, Kamiya H, Komiya N, Odaira F, Sunagawa T, et al. Epidemiology of influenza A(H1N1)v virus infection in Japan, May-June 2009. *Euro Surveill* 2009;14(24).
42. Kawaguchi R, Miyazono M, Noda T, Takayama Y, Sasai Y, Iso H. Influenza (H1N1) 2009 outbreak and school closure, Osaka Prefecture, Japan. *Emerg Infect Dis* 2009;15(10):1685.
43. Chieochansin T, Makkoch J, Suwannakarn K, Payungporn S, Poovorawan Y. Novel H1N1 2009 influenza virus infection in Bangkok, Thailand:Effects of school closures. *Asian Biomedicine* 2009;3(5):469-75.
44. Wu JT, Cowling BJ, Lau EH, Ip DK, Ho LM, Tsang T, et al. School closure and mitigation of pandemic (H1N1) 2009, Hong Kong. *Emerg Infect Dis* 2010;16(3):538-41.
45. Cowling BJ, Lau MSY, Ho LM, Chuang SK, Tsang T, Liu SH, et al. The effective reproduction number of pandemic influenza: Prospective estimation. *Epidemiology* 2010;21(6):842-46.
46. Hsueh P-R, Lee P-I, Hsiang Chiu A-W, Yen M-Y. Pandemic (H1N1) 2009 vaccination and class suspensions after outbreaks, Taipei City, Taiwan. *Emerg Infect Dis* 2010;16(8):1309-11.
47. Wu J, Xu F, Lu L, Lu M, Miao L, Gao T, et al. Safety and effectiveness of a 2009 H1N1 vaccine in Beijing. *New England Journal of Medicine* 2010;363(25):2416-23.
48. Huai Y, Lin J, Varma JK, Peng Z, He J, Cheng C, et al. A primary school outbreak of pandemic 2009 influenza A (H1N1) in China. *Influenza other respi* 2010;4(5):259-66.
49. Engelhard D, Bromberg M, Averbuch D, Tenenbaum A, Goldmann D, Kunin M, et al. Increased extent of and risk factors for pandemic (H1N1) 2009 and seasonal infl uenza among children, Israel. *Emerging Infectious Diseases* 2011;17(9):1740-43.
50. Leung YH, Li MP, Chuang SK. A school outbreak of pandemic (H1N1) 2009 infection: assessment of secondary household transmission and the protective role of oseltamivir. *Epidemiol Infect* 2011;139(1):41-4.

51. Uchida M, Tsukahara T, Kaneko M, Washizuka S, Kawa S. Swine-origin influenza a outbreak 2009 at Shinshu University, Japan. *BMC Public Health* 2011;11:79.
52. Rajatonirina S, Heraud J-M, Randrianasolo L, Razanajatovo N, Ramandimbisoa T, Ratsitorahina M, et al. Pandemic influenza A(H1N1) 2009 virus outbreak among boarding school pupils in Madagascar: compliance and adverse effects of prophylactic oseltamivir treatment. *J* 2011;5(3):156-62.
53. Caley P, Philp DJ, McCracken K. Quantifying social distancing arising from pandemic influenza. *J R Soc Interface* 2008;5(23):631-9.
54. Baker MG, Wilson N, Huang QS, Paine S, Lopez L, Bandaranayake D, et al. Pandemic influenza A(H1N1)v in New Zealand: the experience from April to August 2009. *Euro Surveill* 2009;14(34).
55. Hall RJ, Peacey MP, Ralston JC, Bocacao J, Ziki M, Gunn W, et al. Pandemic influenza A(H1N1)v viruses currently circulating in New Zealand are sensitive to oseltamivir. *Euro Surveill* 2009;14(30):19282.
56. Effler PV, Carcione D, Giele C, Dowse GK, Goggin L, Mak DB. Household responses to pandemic (H1N1) 2009-related school closures, Perth, Western Australia. *Emerg Infect Dis* 2010;16(2):205-11.
57. Paine S, Mercer GN, Kelly PM, Bandaranayake D, Baker MG, Huang QS, et al. Transmissibility of 2009 pandemic influenza A(H1N1) in New Zealand: effective reproduction number and influence of age, ethnicity and importations. *Euro Surveill* 2010;15(24).
58. Cruz-Pacheco G, Duran L, Esteva L, Minzoni A, Lopez-Cervantes M, Panayotaros P, et al. Modelling of the influenza A(H1N1)v outbreak in Mexico City, April-May 2009, with control sanitary measures. *Euro Surveill* 2009;14(26).
59. Echevarria-Zuno S, Mejia-Arangure JM, Mar-Obeso AJ, Grajales-Muniz C, Robles-Perez E, Gonzalez-Leon M, et al. Infection and death from influenza A H1N1 virus in Mexico: a retrospective analysis. *Lancet* 2009.
60. Stern AM, Markel H. What Mexico taught the world about pandemic influenza preparedness and community mitigation strategies. *Jama* 2009;302(11):1221-2.
61. Lajous M, Danon L, Lopez-Ridaura R, Astley CM, Miller JC, Dowell SF, et al. Mobile messaging as surveillance tool during pandemic (H1N1) 2009, Mexico. *Emerg Infect Dis* 2010;16(9):1488-9.
62. Gomez J, Munayco C, Arrasco J, Suarez L, Laguna-Torres V, Aguilar P, et al. Pandemic influenza in a southern hemisphere setting: the experience in Peru from May to September, 2009. *Euro Surveill* 2009;14(42).
63. Tinoco Y, Razuri H, Ortiz EJ, Gomez J, Widdowson MA, Uyeki T, et al. Preliminary population-based epidemiological and clinical data on 2009 pandemic H1N1 influenza A (pH1N1) from Lima, Peru. *Influenza Other Respi Viruses* 2009;3(6):253-6.
64. Lessler J, Reich NG, Cummings DAT, New York City Department of H, Mental Hygiene Swine Influenza Investigation T, Nair HP, et al. Outbreak of 2009 pandemic influenza A (H1N1) at a New York City school. *N Engl J Med* 2009;361(27):2628-36.
65. Miller JC, Danon L, O'Hagan JJ, Goldstein E, Lajous M, Lipsitch M. Student behavior during a school closure caused by pandemic influenza A/H1N1. *PLoS ONE* 2010;5(5):e10425.
66. Janjua NZ, Skowronski DM, Hottes TS, Osei W, Adams E, Petric M, et al. Seasonal influenza vaccine and increased risk of pandemic A/H1N1-related illness: First detection of the association in British Columbia, Canada. *Clinical Infectious Diseases* 2010;51(9):1017-27.

67. Marchbanks TL, Bhattarai A, Fagan RP, Ostroff S, Sodha SV, Moll ME, et al. An outbreak of 2009 pandemic influenza A (H1N1) virus infection in an elementary school in Pennsylvania. *Clin Infect Dis* 2011;52 Suppl 1:S154-60.
68. Cauchemez S, Bhattarai A, Marchbanks TL, Fagan RP, Ostroff S, Ferguson NM, et al. Role of social networks in shaping disease transmission during a community outbreak of 2009 H1N1 pandemic influenza. *Proc Natl Acad Sci U S A* 2011;108(7):2825-30.
69. Janusz KB, Cortes JE, Serdarevic F, Jones RC, Jones JD, Ritger KA, et al. Influenza-like illness in a community surrounding a school-based outbreak of 2009 pandemic influenza A (H1N1) virus-Chicago, Illinois, 2009. *Clin Infect Dis* 2011;52 Suppl 1:S94-101.
70. Cohen NJ, Callahan DB, Gonzalez V, Balaban V, Wang RT, Pordell P, et al. Respiratory illness in households of school-dismissed students during pandemic (H1N1) 2009. *Emerging Infectious Diseases* 2011;17(9):1756-57.
71. Loustalot F, Silk BJ, Gaither A, Shim T, Lamias M, Dawood F, et al. Household transmission of 2009 pandemic influenza A (H1N1) and nonpharmaceutical interventions among households of high school students in San Antonio, Texas. *Clin Infect Dis* 2011;52 Suppl 1:S146-53.
72. Chowell G, Echevarria-Zuno S, Viboud C, Simonsen L, Tamerius J, Miller MA, et al. Characterizing the epidemiology of the 2009 influenza A/H1N1 pandemic in Mexico. *PLoS Med* 2011;8(5):e1000436.
73. Herrera-Valdez MA, Cruz-Aponte M, Castillo-Chavez C. Multiple outbreaks for the same pandemic: Local transportation and social distancing explain the different "Waves" of A-H1N1PDM cases observed in Mexico during 2009. *Mathematical Biosciences and Engineering* 2011;8(1):21-48.
74. Chowell G, Viboud C, Munayco CV, Gomez J, Simonsen L, Miller MA, et al. Spatial and temporal characteristics of the 2009 A/H1N1 influenza pandemic in Peru. *PLoS ONE* 2011;6(6):e21287.
75. Monto AS, Davenport FM, Napier JA, Francis Jr T. Modification of an outbreak of influenza in tecumseh, michigan by vaccination of schookhildren. *J.Infect.Dis* 1970;122(1-2):328-32.
76. Bootsma MC, Ferguson NM. The effect of public health measures on the 1918 influenza pandemic in U.S. cities. *Proc Natl Acad Sci U S A* 2007;104(18):7588-93.
77. Hatchett RJ, Mecher CE, Lipsitch M. Public health interventions and epidemic intensity during the 1918 influenza pandemic. *Proc Natl Acad Sci U S A* 2007;104(18):7582-7.
78. Markel H, Lipman HB, Navarro JA, Sloan A, Michalsen JR, Stern AM, et al. Nonpharmaceutical interventions implemented by US cities during the 1918-1919 influenza pandemic.[Erratum appears in JAMA. 2007 Nov 21;298(19):2264]. *Jama* 2007;298(6):644-54.
79. Jordan EO, Redd DB, Fink EB. Influenza in three Chicago groups. *Public Health Rep* 1919;34(28):1528-45.
80. Armstrong C, Hopkins R. An epidemiological study of the 1920 epidemic of influenza in an isolated rural community. *Public Health Rep* 1921;36(29):1671-702.

# PRISMA 2009 Checklist

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 3 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | NA |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | NA |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 3-4 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 3-4 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | Appendix, p1 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 4 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 4 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 27 (Box 1) |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | NA |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 4 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | NA |

# PRISMA 2009 Checklist



| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | NA |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | NA |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 5, Figure 1 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | Appendix Tables 1 and 2 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | NA |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | NA |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | NA |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | NA |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | NA |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 12 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 12-15 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 15 |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 16-17 |

*From:* Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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# PRISMA 2009 Checklist

# School closures and influenza: systematic review of epidemiological studies


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|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID: | bmjopen-2012-002149.R1 |
| Article Type: | Research |
| Date Submitted by the Author: | 19-Dec-2012 |
| Complete List of Authors: | Jackson, Charlotte; London School of Hygiene and Tropical Medicine,<br>Vynnycky, Emilia; Health Protection Agency,<br>Hawker, Jeremy; Health Protection Agency,<br>Olowokure, Babatunde; Health Protection Agency,<br>mangtani, punam; London School of Hygiene and Tropical Medicine, |
| <b>Primary Subject Heading</b>: | Epidemiology |
| Secondary Subject Heading: | Epidemiology, Infectious diseases, Public health |
| Keywords: | EPIDEMIOLOGY, Epidemiology < INFECTIOUS DISEASES, Public health < INFECTIOUS DISEASES, PUBLIC HEALTH, SYSTEMATIC REVIEWS |
| | |

# School closures and influenza: systematic review of epidemiological studies

Charlotte Jackson[1], Emilia Vynnycky[2], Jeremy Hawker[3], Babatunde Olowokure[3], Punam Mangtani[1]

[1] London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK; [2] Health Protection Agency, Colindale, London NW9 5EQ, UK; [3] Health Protection Agency, 5 St Philips Place, Birmingham B3 2PW, UK

Corresponding author: Charlotte Jackson, Room 113, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT.

Email: charlotte.jackson@lshtm.ac.uk

Tel: +44 (0) 207 927 2209

Word count: 3999

*Abstract*

Objective: To review the effects of school closures on pandemic and seasonal influenza outbreaks.

Design: Systematic review.

Data sources: Medline and Embase, reference lists of identified articles, hand searches of key journals, and additional papers from the authors' collections.

Study selection: Studies were included if they reported on a seasonal or pandemic influenza outbreak coinciding with a planned or unplanned school closure.

Results: Of 2579 papers identified through Medline and Embase, 65 were eligible for inclusion in the review along with 14 identified from other sources. Influenza incidence frequently declined after school closure. The effect was sometimes reversed when schools reopened, supporting a causal role for school closure in reducing incidence. Any benefits associated with school closure appeared to be greatest amongst school-aged children. However, as schools often closed late in the outbreak or other interventions were used concurrently, it was sometimes unclear how much school closure contributed to the reductions in incidence.

Conclusions: School closures appear to have the potential to reduce influenza transmission, but the heterogeneity in the data available means that the optimum strategy (e.g. the ideal length and timing of closure) remains unclear.

## *Introduction*

During the 2009 influenza pandemic, schools were closed in many settings in efforts to reduce transmission. The World Health Organization does not specifically recommend or discourage school closures during an influenza pandemic, as their potential benefits and harms may be context-specific [1], but has suggested that they be considered as part of a mitigation strategy [2]. Their effects on transmission, however, remain poorly understood [3,4]. Closures may be pro-active (occurring before transmission is established in the school) or reactive (a response to a school-based outbreak), and may involve closure of whole school(s) or dismissal of individual classes [4].

A review of the evidence available before the 2009 pandemic concluded that school closures may be beneficial, depending on characteristics such as age-specific attack rates [4]. Here, we review epidemiological studies to assess the effects of school closures on transmission and incidence of seasonal and pandemic influenza, updating and extending previous reviews [2,4] to include data from the 2009 pandemic.

## *Methods*

*Search strategy and selection criteria*

Medline and Embase were searched in January 2012, without language restrictions, for relevant papers published by the end of 2011 (see Appendix for search strategy). *Eurosurveillance* (23 April 2009 to 15 December 2011), *Morbidity and Mortality Weekly Report* (24 April 2009 to 23 December 2011) and *Emerging Infectious Diseases* (April 2009 to December 2011) were hand-searched. Results were supplemented with papers from the reference lists of the articles identified, and papers from the reviewers' collections. An additional Pubmed search (for the words "influenza" and "school") was used to identify relevant papers published during October – December 2011 but not yet listed in Medline or Embase.

Studies were included if they described one or more influenza outbreaks during which schools were initially open and subsequently closed, with or without other interventions. If papers presented several measures of influenza activity, the most specific data were extracted (e.g. data on laboratory-confirmed influenza were extracted in preference to all-cause school absenteeism). Studies which used modelling techniques to assess how school closure affected transmission based on real epidemic curves were eligible; however, predictive modelling studies exploring how school closure might affect a hypothetical outbreak were excluded. English translations (where available) of the titles and abstracts of papers written in other languages were screened, but these papers were not eligible for inclusion. Studies of outbreaks which started during school closure were excluded.

Abstracts and full text were screened initially by one reviewer and by a second reviewer if necessary. Box 1 summarises the information extracted from the studies. Where possible, epidemic curves were plotted by transcribing daily or weekly data from figures or tables.

*Data analysis*

We summarised the data graphically and descriptively. We plotted the peak and cumulative attack rates (and 95% confidence intervals, calculated using standard methods for calculating CIs for proportions) for each study that provided an appropriate denominator. We calculated the normalised peak (peak AR / median AR) for datasets with a median AR greater than zero, to adjust approximately for differences in case definitions (this approach has been used elsewhere to adjust for intercity differences in case fatality proportions [5]). These estimates were stratified by the timing of closure, i.e. whether schools closed before, coincident with, or after the peak.

### *Results*

Of 2579 papers identified through Medline and Embase, 430 were reviewed in full. 65 of these studies were included in the review, along with 14 additional papers (Figure 1; the supplementary PubMed search yielded no further eligible articles). 79 papers were thus included in the review: 23 for seasonal and 56 for pandemic influenza (49, one, and seven from the 2009, 1968 and 1918 pandemics, respectively). Details of the studies are given in Table 1 and Supplementary Tables 1 and 2.

*Description of the epidemics*

19 and 41 epidemic curves were available on seasonal and pandemic influenza, respectively (Supplementary Figures 1 and 2). School closure was often followed by a reduction in incidence, in children specifically or the general population. However, closure often occurred late in the outbreaks (Table 1), and it is unclear whether it influenced the decline.

The cumulative and peak ARs varied widely for seasonal and pandemic influenza (Figure 2). Normalised peaks partly account for differences in case definitions between studies, but also varied considerably (Figure 3). There was no clear pattern in the cumulative, peak or normalised peak ARs plotted by timing of closure in relation to the peak. Relatively few schools closed before the peak (Figures 2 and 3); of those that did, two also reopened before the peak [6 7]. However, early introduction of non-pharmaceutical interventions (NPIs), which often included school closures, in US cities during the 1918 pandemic has been found to be associated with a reduction in mortality [5 8 9]. In Connecticut in 1918, three cities which closed schools experienced higher mortality rates than two which did not [10].

*Age-specific effects of school closure*

The available age-specific data suggested that any benefits associated with school closure were greatest amongst school-aged children [11-25]. In New Zealand during the 2009 pandemic, the age-standardised proportion of confirmed cases in 5-19 year-olds fell during the winter holiday and increased when schools reopened [19]; a slight increase in ILI consultation rates when schools reopened was confined to 5-14 year-olds [14]. Similar relationships between school closure and the ratio of the number of H1N1 infections in 5-20 year-olds to that in other age groups were reported for Mexico [23] and Peru [26]. During the 1967-68 influenza season in Great Britain, GP consultation rates for ILI amongst 5-14 year-olds declined during the Christmas holiday and increased when schools reopened; this effect was less clear in other age groups [17].

Winter holidays in Israel were associated with a reduction in the ratio between the number of clinic visits for influenza and those for non-respiratory complaints, in 6-12 year-olds, in three of five seasonal influenza periods studied [15]. In one season, this ratio was also reduced in adults, and in another it was reduced for adults not living with 6-12 year-olds. When a two-week teachers' strike coincided with an influenza outbreak in January 2000, closing 80% of elementary schools nationwide, this ratio decreased by 15% for 6-12 year-olds (95% CI 6-23%), but not for older individuals. As the authors note, children comprise a high proportion (34%) of the Israeli population, which may contribute to any apparent benefit of closing schools in Israel [27].

Similar data from four influenza seasons in Arizona are less consistent, partly because school closure rarely coincided with elevated influenza activity [18]. During all four seasons, rates of laboratory-confirmed influenza in school-aged children were similar during the two week winter holiday and the preceding two weeks. In two seasons this rate increased in the two weeks after schools reopened; in one other season, it was significantly lower on reopening than during closure [18]. In comparison, rates in adults and pre-school-aged children increased successively (though not always significantly) across the three two-week periods in three of the seasons [18].

Three studies which fitted transmission models to surveillance data also concluded that school closures mainly benefit children [12 13]. Analyses of French seasonal ILI data [13] and ILI data from London during the 2009 pandemic [22] estimated that school holidays did not affect adults' contact patterns; similarly, reductions in transmission following school closures in Hong Kong in 2009 occurred primarily amongst children [12].

However, two studies of the 2009 pandemic suggested that school closure affected incidence in adults. One of these studies estimated the age-specific number of ILI cases due to pandemic H1N1 in England; in most age groups, these estimated case numbers decreased during the summer holiday and increased when schools reopened [25]. In Vojvodina, Serbia, incidence decreased amongst 5-14 and 15-64 year-olds during a one-week school closure [28].

*Reversibility of effects*

Incidence sometimes rebounded when schools reopened, suggesting that school closure contributed to reducing incidence in some settings. For example, during the 2009 pandemic in England, the estimated weekly number of infections declined during the school summer holiday; a second wave occurred when schools reopened (Supplementary Figure 2) [22 29]. Similar reversibility appeared in ILI consultation rates in Vojvodina in 2009 [28]. Datasets from the 2009 pandemic in Mexico [23 30 31] also suggested an increase in incidence after schools reopened (Supplementary Figure 2). Analyses of NPIs (usually including school closures) during the 1918 pandemic found that, in the cities studied, second waves occurred only after NPIs were lifted [5 8].

In the Israeli data regarding seasonal influenza and the teachers' strike, the number of physician visits for acute respiratory illness was 42% lower during the closure compared to the previous two weeks; incidence increased after the strike [27]. During the 1999-2000 influenza season in Japan, the increase in incidence appeared to slow during the two week winter holiday and accelerated when schools reopened [7]. Similarly, in Beijing in 2009, the cumulative incidence of laboratory-confirmed H1N1 influenza increased more markedly before and after a national school holiday than during the break [32].

*Changes in transmission patterns from modelling analyses of epidemic data*

Several studies have fitted transmission models to observed epidemic data to estimate the reduction in contact rates associated with school closure. School holidays were estimated to reduce transmission of seasonal influenza amongst children by a median of 24% (range 20-29%), based on rates of ILI in France from 1985 to 2006, corresponding to a 16-18% reduction in total case numbers [13]. During the 2009 pandemic in London, contact amongst 5-14 year-olds was reduced by an estimated 72% during the six-week summer holiday; the corresponding reduction during one-week half term holidays was 48% [22]. In US cities in 1918, changes in mortality were attributed to a combination of formal interventions (including school closure) and spontaneous social distancing [8]. In Sydney in 1918, formal and spontaneous social distancing together were estimated to have reduced contact rates by up to 38% [33]. Based on influenza incidence data from the 2009 pandemic in Mexico City, school closure together with other interventions appeared to reduce the population contact rate by 23% [31]. A subsequent analysis of national data from Mexico estimated that the contact rate was reduced by 30% during the intervention period [23].

In Hong Kong (also during the 2009 pandemic), closing primary schools, kindergartens, and childcare centres pro-actively, together with affected secondary schools, was estimated to reduce transmission by 70% amongst children and 25% in the population overall [12]. The same study estimated the effective reproduction number ($R_n$, the average number of secondary infectious persons generated by a single infectious person in a given population) as 1·7 before school closure, 1·5 during school closure, and 1·1 during the subsequent school holidays [12]. Daily estimates of $R_n$ in Hong Kong in 2009 (based on a longer time series) also suggested a decline during school closure and a slight increase following reopening [34].

Modelling techniques have also been used to estimate daily values of $R_n$ during a seasonal influenza outbreak in Hong Kong [35] and the 2009 pandemic in Mexico City [23 31] and New Zealand [19]. The Hong Kong analysis for seasonal influenza suggested that $R_n$ was not substantially affected by school closure, perhaps because closure occurred late in the outbreak when $R_n$ was already below one [35]. In Mexico City [31] and New Zealand, $R_n$ was declining before schools closed and continued to decrease during closure; in New Zealand, $R_n$ increased briefly but not substantially when schools reopened [19]. Analysis of a further outbreak in the USA detected no clear effect of school closure on transmission, which was attributed to the late timing of closure [20].

Modelling analyses of the spatiotemporal spread of pandemic H1N1 in Europe in 2009 were able to reproduce observed incidence patterns only when contact rates were allowed to change specifically during each country's school holidays (holidays were assumed to eliminate transmission in schools and increase community transmission by a factor of 1.4) [36]. In all countries, holidays were estimated to delay the peak compared to a hypothetical situation without school closure. In contrast, regression analysis of estimates of $R_n$ in 12 European countries found no evidence of an effect of school holidays on transmission in the nine countries in which school holidays coincided with the study period [37]. The authors proposed that this apparent lack of effect might result from changes in reporting, stochastic effects early in the outbreaks, and the fact that in some countries (including England), school holidays occurred outside the study period.

*Different school closure strategies*

In some outbreaks, individual schools were closed; in others, school closure was more widespread (Supplementary Tables 1 and 2). The effects of these different strategies could not be compared, due to both late implementation and differences between the studies in other factors (such as the duration of closure).

Analyses of the 1918 pandemic in US cities found that the duration of NPIs was negatively associated with the total excess death rate [9]. In the datasets reviewed here, closures longer than two weeks were associated with reduced incidence or transmission in several studies of seasonal [38] and pandemic [12 29] influenza, but not in others [11 39]. Two studies which suggested reasonably strong evidence of an effect of school closure (from France and Israel) reported on closures lasting two weeks [13 27]. Studies in Japan [7] and England and Wales [17] also suggested possible effects of two-week closures on seasonal influenza. However, closures of this length did not always appear to reduce transmission [35]. Shorter closures, e.g. of 1-2 weeks, may sometimes have contributed to reductions in transmission [22 29 31 32 40], but often had no obvious effect [41-44]. In London, contacts between children were reduced more dramatically during a six-week holiday than during one-week breaks, but this may reflect different behaviour during the different holidays [22].

*Use of multiple interventions*

In most of the pandemic influenza studies, other interventions were implemented alongside school closure and may have contributed to any reduction in incidence. In 2009, antiviral treatment and / or prophylaxis was commonly used in the studies identified [12 14 19 20 39 40 42 45-57]. Public places were sometimes closed and / or large gatherings were discouraged or restricted [16 30 31 58]. Some datasets from the 2009 pandemic included vaccination against the pandemic strain, although this was usually only available late in the study period so would not affect the included incidence data [29 32 57 59]. In 1918, school closures were often combined with other social distancing measures [5 8 9 33]; the only study included from the 1968 pandemic was a vaccine trial [60]. Of the few pandemic studies which mentioned no additional interventions, one suggested an effect of school closures: in Israel in 2009, three waves of infection corresponded to the planned closure and reopening of schools [61]. In the England and Wales data for the 2009 pandemic, other interventions (vaccination and antivirals) were used to only a limited extent; incidence still clearly declined during the school summer holiday and increased afterwards [29].

Some studies of seasonal influenza mentioned additional interventions (e.g. vaccination [62-64], prophylactic amantadine [65], hygiene promotion [38 41 66], closure of public places [38], and advice

to avoid large gatherings [44]). However, some studies without additional interventions showed reductions in incidence and / or transmission during school closure [13 27].

*Discussion*

This systematic review of the effects of school closures on influenza outbreaks extends previous reviews [2 4] to include published experiences from the 2009 pandemic. The results suggest that school closure can reduce transmission of pandemic [12] and seasonal [13 27] influenza amongst schoolchildren. Many datasets, however, show no clear effect of school closure. As noted by some authors [20 43 44], this may sometimes have been because schools shut late in the outbreak (often close to or after the peak).

In some studies, incidence increased when schools reopened [5 7 8 14 22 27 29 31]. This apparent reversibility provides evidence that school closure can cause reductions in influenza incidence. In two of the studies of seasonal influenza which showed reversibility [7 27], no additional interventions (beyond usual seasonal interventions) were used. In many other datasets, multiple interventions were used, so the specific effects of school closures are difficult to isolate.

In 2009, several countries closed schools whilst in others, planned holidays coincided with outbreaks. Several datasets from this pandemic strengthen support for school closure as an intervention; however, others illustrate that benefits are not guaranteed and that timely closure may be challenging. The sensitivity of the 2009 pandemic to school closures probably reflects the age-specific attack rates, which were higher in children than adults; outbreaks in which children are less affected might be less sensitive to school closure.

Studies presenting age-stratified data suggested that the effects of school closure on transmission were greater amongst children than adults. Few studies stratified children further, e.g. into primary and secondary school students. Older children might socialise more than younger children during school closures, so closing primary schools may have a greater effect on transmission than closing secondary schools (e.g. in Hong Kong in 2009, primary schools were closed pro-actively whilst secondary schools closed if cases occurred amongst their students [12]).

The long term effects of closing schools are unclear, as relatively few of the studies presented substantial data after schools reopened. For example, school closure could result in multiple peaks, potentially involving more cases than would otherwise have occurred [8]. However, a study published since this review was conducted estimated that case numbers in Alberta, Canada, could have been up to twice as high as those seen if schools had not closed for planned holidays [67]. It is difficult to compare reactive versus pro-active closures, different durations of closure, and local versus national closures as studies typically differed in several respects. Age-specific data suggest that the effects of school closure are greatest among school-aged children [12-15 17 22].

Some studies have concluded that reopening schools after holiday periods can accelerate epidemic growth (e.g. during the 1957 [68 69] and 2009 [70] pandemics). These studies were beyond the scope of this review of the effects of closing schools after outbreaks have started, but they suggest that extending school holidays might delay the spread of an epidemic beginning during a break.

Results from analyses of seasonal influenza may not be directly applicable to a pandemic. Schools were often closed for planned holidays rather than in response to the outbreaks; contact patterns may differ between reactive school closures [71] and holidays [72]. Extrapolating from previous pandemics may also be problematic. Modelling studies [73-75] have predicted that school closures will have the greatest effects if transmission occurs mainly amongst children. The importance of children in transmission has varied between pandemics [76]; in 2009, attack rates were higher in children than in adults, probably because of pre-existing immunity in older individuals [77]. Viral virulence will also influence individuals' responses to school closure and other interventions, e.g. spontaneous social distancing during a mild pandemic may be less dramatic than occurred in 1918. Changes in household size, contact patterns, children's behaviour and school systems since 1918, 1957 and 1968 may also limit the generalisability of experiences from these pandemics. As noted in a study of the 1918 pandemic in Connecticut, reverse causality may occur when comparing rates in cities which closed schools to those in cities which did not, if closure was a response to a particularly severe local outbreak [10].

One limitation of the datasets is that ascertainment may have changed during the outbreaks, due to changes in surveillance and care-seeking behaviour. Increases in ascertainment during an outbreak could obscure any reductions in incidence during school closures (e.g. in one study, enhanced surveillance began the day the school closed [56]). Conversely, the proportion of patients who undergo virological testing may be reduced late in an outbreak, and in some settings (e.g. New Zealand [14]) patients with ILI were discouraged from consulting GPs during the 2009 pandemic. The estimated proportion of influenza cases that were reported in Hong Kong declined to ~5% of its original value during the move from containment to mitigation during the 2009 pandemic [12]. In England, the introduction of the National Pandemic Flu

Service telephone helpline coincided with the school holiday, and was estimated to have reduced the probability of GP consultation for adults with ILI from 16% to 1.8% [22].

Case definitions may not always have been well-suited to detecting any effect of school closure. For example, school absenteeism is a relatively non-specific measure, whilst laboratory specimens frequently represent severe infections (e.g. in the elderly, who may have little contact with children and therefore be relatively unaffected by school closure).

Influenza transmission is influenced by factors besides contact in schools, including temperature and absolute humidity (AH) [78-81]. Two studies which assessed the role of AH during the 2009 pandemic did not find strong evidence that it affected transmission [24 37]. The two waves seen in the UK in 2009 could be explained by changes in contact patterns during school holidays [29 82]. In a modelling study of data from Alberta, Canada, the best-fitting model included effects of temperature and school holidays on transmission, and predicted that if schools had not closed, the outbreak would have been restricted by temperature effects but would still have been 2.1 times larger than was observed in the province as a whole (1.38 and 1.54 times in the cities of Calgary and Edmonton, respectively) [67]. A study of the interplay between school calendars, AH and population susceptibility in enhancing influenza transmission concluded that high AH may prevent influenza outbreaks [79]. However, if a sufficiently high proportion of the population is susceptible, outbreaks can occur even when AH is high; the opening of schools may enhance transmission [79]. Taken together, these studies suggest that contact in schools is not the only determinant of influenza transmission, but it is one influential (and modifiable) factor.

Previous studies have attempted to estimate the effects of public health interventions using transmission models [8 12 20 31]. The development of such models is complicated for the datasets reviewed here, and would not necessarily have provided conclusive insight into the impact of school closures. For example, many factors are unknown and would need to be estimated or assumed for each dataset, such as the basic reproduction number, proportion of infections that were reported, the effect of other interventions, and the proportion of individuals who were immune at the start of the outbreak.

The review was limited to published studies, which could potentially introduce publication bias. However, many of the studies identified did not aim to evaluate the effects of school closure on transmission, so publication bias appears unlikely. This is supported by the apparent lack of an effect of school closure in many of the studies (including some of those which did specifically assess school closure as an intervention). Foreign language papers were excluded, but in most cases it was clear from the title and / or abstract (available in English) that the papers were not relevant to this review.

***Conclusions***

The available data suggest that school closures can potentially reduce transmission during an influenza outbreak, even in the absence of other interventions, although the optimal school closure strategy is unclear. The effect of school closures is larger for school-aged children than for other age groups, although there is some evidence that incidence in adults might also be reduced. During a future pandemic (or seasonal outbreaks during which schools are closed), it will be important to collect incidence data using systematic ascertainment and a consistent case definition, before, during and after school closure, to assess the effects of school closures on transmission. Analysis of comparable data from multiple outbreaks may help to overcome some of the problems with comparability and ascertainment discussed above, and clarify which features determine the effectiveness of school closures. Although timely school closures may reduce transmission, other implications of school closure (e.g. ethical and economic considerations) [4], and viral properties such as virulence, must also be considered in policy decisions, and may depend on the local context [1].

***Summary***

*Article focus*

- This systematic review assesses the effects of school closures on transmission of influenza, including data from the recent 2009 pandemic as well as from previous pandemics and seasonal outbreaks.

*Key messages*

- The available data suggest that school closure can be a useful intervention during influenza outbreaks, with the greatest benefits occurring amongst school-aged children.

*Strengths and limitations*

- We have reviewed an extensive body of literature on the effects of school closure on the incidence and transmission of influenza.
- The optimum timing and duration of closure are unclear because studies often differed in several respects, or used other interventions in addition to school closure.

*Acknowledgements*

This paper developed from a review commissioned by the UK Health Protection Agency as part of its pandemic influenza programme. We thank Nadia Inglis, Angus Nicoll and two anonymous members of the HPA's Influenza and Respiratory Virus Programme Board for helpful comments on the review. We also thank staff at the LSHTM library for assistance in locating papers.

*Funding*

This work was partially funded by the Health Protection Agency; C.J. was supported by a Research Training Fellowship from the National Institute for Health Research.

*Role of the funding source*

NIHR had no role in the design and conduct of the study; collection, analysis or interpretation of data; writing of the report; or the decision to submit the article for publication. The HPA commissioned the research.

*Access to data*

All authors had full access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

*Data sharing*

No additional data available.

*Competing interest statement*

All authors have completed the Unified Competing Interest form at http://www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: funding from NIHR and HPA; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

*Statement of authors' roles*

B.O and J.H. had the initial idea. P.M., C.J. and E.V. developed the research questions and study design. C.J. carried out the literature review and P.M. assessed any doubtful papers. C.J., P.M. and E.V. analysed data. C.J., P.M. and E.V. wrote the paper. J.H. commented on outputs and contributed to the final draft. J.H. and B.O. contributed to the final draft.

*Ethical approval*

Not required.

***References***


1. World Health Organization. Reducing transmission of pandemic (H1N1) 2009 in school settings. A framework for national and local planning and response, 2009.
2. Bell DM, World Health Organization Writing Group. Non-pharmaceutical interventions for pandemic influenza, national and community measures. *Emerg Infect Dis* 2006;12(1):88-94.
3. Aledort JE, Lurie N, Wasserman J, Bozzette SA. Non-pharmaceutical public health interventions for pandemic influenza: an evaluation of the evidence base. *BMC Public Health* 2007;7:208.
4. Cauchemez S, Ferguson NM, Wachtel C, Tegnell A, Saour G, Duncan B, et al. Closure of schools during an influenza pandemic. *The Lancet Infectious Diseases* 2009;9(8):473-81.
5. Hatchett RJ, Mecher CE, Lipsitch M. Public health interventions and epidemic intensity during the 1918 influenza pandemic. *Proc Natl Acad Sci U S A* 2007;104(18):7582-7.
6. Olson JG. School absenteeism during an outbread of B/Hong Kong/5/72-like influenze virus in Taipei, Taiwan. *Southeast Asian J Trop Med Public Health* 1980;11(4):429-34.
7. Fujii H, Takahashi H, Ohyama T, Hattori K, Suzuki S. Evaluation of the school health surveillance system for influenza, Tokyo, 1999-2000. *Japanese Journal of Infectious Diseases* 2002;55(3):97-98.
8. Bootsma MC, Ferguson NM. The effect of public health measures on the 1918 influenza pandemic in U.S. cities. *Proc Natl Acad Sci U S A* 2007;104(18):7588-93.
9. Markel H, Lipman HB, Navarro JA, Sloan A, Michalsen JR, Stern AM, et al. Nonpharmaceutical interventions implemented by US cities during the 1918-1919 influenza pandemic.[Erratum appears in JAMA. 2007 Nov 21;298(19):2264]. *Jama* 2007;298(6):644-54.
10. Winslow C-EA, Rogers JF. Statistics of the 1918 Epidemic of Influenza in Connecticut: With a consideration of the factors which influenced the prevalence of this disease in various communities *J Infect Dis* 1920;26(3):185-216.
11. Armstrong C, Hopkins R. An epidemiological study of the 1920 epidemic of influenza in an isolated rural community. *Public Health Reports* 1921;36(29):1671-702.
12. Wu JT, Cowling BJ, Lau EH, Ip DK, Ho LM, Tsang T, et al. School closure and mitigation of pandemic (H1N1) 2009, Hong Kong. *Emerg Infect Dis* 2010;16(3):538-41.
13. Cauchemez S, Valleron A-J, Boelle P-Y, Flahault A, Ferguson NM. Estimating the impact of school closure on influenza transmission from Sentinel data. *Nature* 2008;452(7188):750-4.
14. Baker MG, Wilson N, Huang QS, Paine S, Lopez L, Bandaranayake D, et al. Pandemic influenza A(H1N1)v in New Zealand: the experience from April to August 2009. *Euro Surveill* 2009;14(34).
15. Heymann AD, Hoch I, Valinsky L, Kokia E, Steinberg DM. School closure may be effective in reducing transmission of respiratory viruses in the community. *Epidemiol Infect* 2009;137(10):1369-76.
16. Tinoco Y, Razuri H, Ortiz EJ, Gomez J, Widdowson MA, Uyeki T, et al. Preliminary population-based epidemiological and clinical data on 2009 pandemic H1N1 influenza A (pH1N1) from Lima, Peru. *Influenza Other Respi Viruses* 2009;3(6):253-6.
17. Miller DL, Lee JA. Influenza in Britain 1967-68. *Journal of Hygiene* 1969;67:559-72.

18. Wheeler CC, Erhart LM, Jehn ML. Effect of school closure on the incidence of influenza among school-age children in Arizona. *Public Health Rep* 2010;125(6):851-9.
19. Paine S, Mercer GN, Kelly PM, Bandaranayake D, Baker MG, Huang QS, et al. Transmissibility of 2009 pandemic influenza A(H1N1) in New Zealand: effective reproduction number and influence of age, ethnicity and importations. *Euro Surveill* 2010;15(24).
20. Cauchemez S, Bhattarai A, Marchbanks TL, Fagan RP, Ostroff S, Ferguson NM, et al. Role of social networks in shaping disease transmission during a community outbreak of 2009 H1N1 pandemic influenza. *Proc Natl Acad Sci U S A* 2011;108(7):2825-30.
21. Marchbanks TL, Bhattarai A, Fagan RP, Ostroff S, Sodha SV, Moll ME, et al. An outbreak of 2009 pandemic influenza A (H1N1) virus infection in an elementary school in Pennsylvania. *Clin Infect Dis* 2011;52 Suppl 1:S154-60.
22. Birrell PJ, Ketsetzis G, Gay NJ, Cooper BS, Presanis AM, Harris RJ, et al. Bayesian modeling to unmask and predict influenza A/H1N1pdm dynamics in London. *Proceedings of the National Academy of Sciences of the United States of America* 2011;108(45):18238-43.
23. Chowell G, Echevarria-Zuno S, Viboud C, Simonsen L, Tamerius J, Miller MA, et al. Characterizing the epidemiology of the 2009 influenza A/H1N1 pandemic in Mexico. *PLoS Med* 2011;8(5):e1000436.
24. Chowell G, Viboud C, Munayco CV, Gomez J, Simonsen L, Miller MA, et al. Spatial and temporal characteristics of the 2009 A/H1N1 influenza pandemic in Peru. *PLoS ONE* 2011;6(6):e21287.
25. Evans B, Charlett A, Powers C, McLean E, Zhao H, Bermingham A, et al. Has estimation of numbers of cases of pandemic influenza H1N1 in England in 2009 provided a useful measure of the occurrence of disease? *Influenza and other Respiratory Viruses* 2011;5(6):e504-e12.
26. Munayco CV, Gomez J, Laguna-Torres VA, Arrasco J, Kochel TJ, Fiestas V, et al. Epidemiological and transmissibility analysis of influenza A(H1N1)v in a southern hemisphere setting: Peru. *Euro surveillance : bulletin europeen sur les maladies transmissibles = European communicable disease bulletin* 2009;14(32).
27. Heymann A, Chodick G, Reichman B, Kokia E, Laufer J. Influence of school closure on the incidence of viral respiratory diseases among children and on health care utilization. *Pediatr Infect Dis J* 2004;23(7):675-7.
28. Petrovic V, Seguljev Z, Cosic G, Ristic M, Nedeljkovic J, Dragnic N, et al. Overview of the winter wave of 2009 pandemic influenza A(H1N1)v in Vojvodina, Serbia. *Croatian Medical Journal* 2011;52(2):141-50.
29. Baguelin M, Hoek AJV, Jit M, Flasche S, White PJ, Edmunds WJ. Vaccination against pandemic influenza A/H1N1v in England: A real-time economic evaluation. *Vaccine* 2010;28(12):2370-84.
30. Echevarria-Zuno S, Mejia-Arangure JM, Mar-Obeso AJ, Grajales-Muniz C, Robles-Perez E, Gonzalez-Leon M, et al. Infection and death from influenza A H1N1 virus in Mexico: a retrospective analysis. *Lancet* 2009.
31. Cruz-Pacheco G, Duran L, Esteva L, Minzoni A, Lopez-Cervantes M, Panayotaros P, et al. Modelling of the influenza A(H1N1)v outbreak in Mexico City, April-May 2009, with control sanitary measures. *Euro Surveill* 2009;14(26).
32. Wu J, Xu F, Lu L, Lu M, Miao L, Gao T, et al. Safety and effectiveness of a 2009 H1N1 vaccine in Beijing. *New England Journal of Medicine* 2010;363(25):2416-23.
33. Caley P, Philp DJ, McCracken K. Quantifying social distancing arising from pandemic influenza. *Journal of the Royal Society Interface* 2008;5(23):631-9.

34. Cowling BJ, Lau MSY, Ho LM, Chuang SK, Tsang T, Liu SH, et al. The effective reproduction number of pandemic influenza: Prospective estimation. *Epidemiology* 2010;21(6):842-46.
35. Cowling BJ, Lau EHY, Lam CLH, Cheng CKY, Kovar J, Chan KH, et al. Effects of school closures, 2008 winter influenza season, Hong Kong. *Emerg Infect Dis* 2008;14(10):1660-2.
36. Merler S, Ajelli M, Pugliese A, Ferguson NM. Determinants of the spatiotemporal dynamics of the 2009 H1N1 pandemic in europe: Implications for real-time modelling. *PLoS Computational Biology* 2011;7(9).
37. Flasche S, Hens N, Boëlle P-Y, Mossong J, van Ballegooijen WM, Nunes B, et al. Different transmission patterns in the early stages of the influenza A(H1N1)v pandemic: A comparative analysis of 12 European countries. *Epidemics* 2011;3(2):125-33.
38. Lo JY, Tsang TH, Leung YH, Yeung EY, Wu T, Lim WW. Respiratory infections during SARS outbreak, Hong Kong, 2003. *Emerg Infect Dis* 2005;11(11):1738-41.
39. Gomez J, Munayco C, Arrasco J, Suarez L, Laguna-Torres V, Aguilar P, et al. Pandemic influenza in a southern hemisphere setting: the experience in Peru from May to September, 2009. *Euro Surveill* 2009;14(42).
40. Kawaguchi R, Miyazono M, Noda T, Takayama Y, Sasai Y, Iso H. Influenza (H1N1) 2009 outbreak and school closure, Osaka Prefecture, Japan. *Emerg Infect Dis* 2009;15(10):1685.
41. Danis K, Fitzgerald M, Connell J, Conlon M, Murphy PG. Lessons from a pre-season influenza outbreak in a day school. *Commun Dis Public Health* 2004;7(3):179-83.
42. Calatayud L, Kurkela S, Neave PE, Brock A, Perkins S, Zuckerman M, et al. Pandemic (H1N1) 2009 virus outbreak in a school in London, April-May 2009: an observational study. *Epidemiol Infect* 2010;138(2):183-91.
43. Rodriguez CV, Rietberg K, Baer A, Kwan-Gett T, Duchin J. Association between school closure and subsequent absenteeism during a seasonal influenza epidemic. *Epidemiology* 2009;20(6):787-92.
44. Johnson AJ, Moore ZS, Edelson PJ, Kinnane L, Davies M, Shay DK, et al. Household responses to school closure resulting from outbreak of influenza B, North Carolina. *Emerg Infect Dis* 2008;14(7):1024-30.
45. Smith A, Coles S, Johnson S, Saldana L, Ihekweazu C, O'Moore E. An outbreak of influenza A(H1N1)v in a boarding school in South East England, May-June 2009. *Euro Surveill* 2009;14(27):9.
46. Effler PV, Carcione D, Giele C, Dowse GK, Goggin L, Mak DB. Household responses to pandemic (H1N1) 2009-related school closures, Perth, Western Australia. *Emerg Infect Dis* 2010;16(2):205-11.
47. Health Protection Agency West Midlands H1N1v Investigation Team. Preliminary descriptive epidemiology of a large school outbreak of influenza A(H1N1)v in the West Midlands, United Kingdom, May 2009. *Euro Surveill* 2009;14(27).
48. Wallensten A, Oliver I, Lewis D, Harrison S. Compliance and side effects of prophylactic oseltamivir treatment in a school in South West England. *Euro Surveill* 2009;14(30):19285.
49. Strong M, Burrows J, Stedman E, Redgrave P. Adverse drug effects following oseltamivir mass treatment and prophylaxis in a school outbreak of 2009 pandemic influenza A(H1N1) in June 2009, Sheffield, United Kingdom. *Euro Surveill* 2010;15(19):pii/19565.

50. Guinard A, Grout L, Durand C, Schwoebel V. Outbreak of influenza A(H1N1)v without travel history in a school in the Toulouse district, France, June 2009. *Euro Surveill* 2009;14(27).
51. France AM, Jackson M, Schrag S, Lynch M, Zimmerman C, Biggerstaff M, et al. Household transmission of 2009 influenza A (H1N1) virus after a school-based outbreak in New York City, April-May 2009. *J Infect Dis* 2010;201(7):984-92.
52. Lessler J, Reich NG, Cummings DAT, New York City Department of H, Mental Hygiene Swine Influenza Investigation T, Nair HP, et al. Outbreak of 2009 pandemic influenza A (H1N1) at a New York City school. *N Engl J Med* 2009;361(27):2628-36.
53. Nishiura H, Castillo-Chavez C, Safan M, Chowell G. Transmission potential of the new influenza A(H1N1) virus and its age-specificity in Japan. *Euro Surveill* 2009;14(22):4.
54. Shimada T, Gu Y, Kamiya H, Komiya N, Odaira F, Sunagawa T, et al. Epidemiology of influenza A(H1N1)v virus infection in Japan, May-June 2009. *Euro Surveill* 2009;14(24).
55. Carrillo-Santisteve P, Renard-Dubois S, Cheron G, Csaszar-Goutchkoff M, Lecuit M, Lortholary O, et al. 2009 pandemic influenza A(H1N1) outbreak in a complex of schools in Paris, France, June 2009. *Euro Surveill* 2010;15(25):24.
56. Huai Y, Lin J, Varma JK, Peng Z, He J, Cheng C, et al. A primary school outbreak of pandemic 2009 influenza A (H1N1) in China. *Influenza other respi* 2010;4(5):259-66.
57. Poggensee G, Gilsdorf A, Buda S, Eckmanns T, Claus H, Altmann D, et al. The first wave of pandemic influenza (H1N1) 2009 in Germany: From initiation to acceleration. *BMC Infectious Diseases* 2010;10(155).
58. Miller JC, Danon L, O'Hagan JJ, Goldstein E, Lajous M, Lipsitch M. Student behavior during a school closure caused by pandemic influenza A/H1N1. *PLoS ONE* 2010;5(5):e10425.
59. Hsueh P-R, Lee P-I, Hsiang Chiu A-W, Yen M-Y. Pandemic (H1N1) 2009 vaccination and class suspensions after outbreaks, Taipei City, Taiwan. *Emerg Infect Dis* 2010;16(8):1309-11.
60. Monto AS, Davenport FM, Napier JA, Francis Jr T. Modification of an outbreak of influenza in tecumseh, michigan by vaccination of schookhildren. *J.Infect.Dis* 1970;122(1-2):328-32.
61. Engelhard D, Bromberg M, Averbuch D, Tenenbaum A, Goldmann D, Kunin M, et al. Increased extent of and risk factors for pandemic (H1N1) 2009 and seasonal infl uenza among children, Israel. *Emerging Infectious Diseases* 2011;17(9):1740-43.
62. Briscoe JH. The protective effect of influenza vaccine in a mixed influenza A and B epidemic in a boys' boarding school. *J R Coll Gen Pract* 1977;27(166):28-31.
63. Farley TA, St. Germain JM, Chamberlain LA, Krassner L. The impact of influenza vaccination on respiratory illness at a boarding School. *Journal of American College Health* 1992;41(3):127-31.
64. Sonoguchi T, Naito H, Hara M. Cross-subtype protection in humans during sequential, overlapping, and/or concurrent epidemics caused by H3N2 and H1N1 influenza viruses. *Journal of Infectious Diseases* 1985;151(1):81-88.
65. Davies JR, Grilli EA, Smith AJ, Hoskins TW. Prophylactic use of amantadine in a boarding school outbreak of influenza A. *J R Coll Gen Pract* 1988;38(313):346-8.
66. Cashman P, Massey P, Durrheim D, Islam F, Merritt T, Eastwood K. Pneumonia cluster in a boarding school--implications for influenza control. *Commun Dis Intell* 2007;31(3):296-8.

67. Earn DJ, He D, Loeb MB, Fonseca K, Lee BE, Dushoff J. Effects of school closure on incidence of pandemic influenza in Alberta, Canada. *Ann Intern Med* 2012;156(3):173-81.
68. Brunyate WDT, Fleming GM, Llopis A, Roden AT. The early stages of the 1957 influenza epidemic in England and Wales in relation to the re-assembly of schools. *Mon Bull Minist Hlth Lab Serv* 1961;20(MAY):88-92.
69. Dunn FL, Carey DE, Cohen A, Martin JD. Epdemiologic studies of asian influenza in a louisiana parish. *Amer* 1959;J.Hyg. 70(3):351-71.
70. Chao DL, Halloran ME, Longini IM, Jr. School opening dates predict pandemic influenza A(H1N1) outbreaks in the United States. *J Infect Dis* 2010;202(6):877-80.
71. Jackson C, Mangtani P, Vynnycky E, Fielding K, Kitching A, Mohamed H, et al. School Closures and Student Contact Patterns. *Emerg Infect Dis* 2011;17(2):245-47.
72. Eames KTD, Tilston NL, White PJ, Adams E, Edmunds WJ. The impact of illness and the impact of school closure on social contact patterns. *Health Technol Assess* 2010;14(34):267-312.
73. Glass K, Barnes B. How much would closing schools reduce transmission during an influenza pandemic? *Epidemiology* 2007;18(5):623-8.
74. Vynnycky E, Edmunds WJ. Analyses of the 1957 (Asian) influenza pandemic in the United Kingdom and the impact of school closures. *Epidemiol Infect* 2008;136(2):166-79.
75. Milne GJ, Kelso JK, Kelly HA, Huband ST, McVernon J. A small community model for the transmission of infectious diseases: comparison of school closure as an intervention in individual-based models of an influenza pandemic. *PLoS ONE* 2008;3(12):e4005.
76. Davis LE, Caldwell GG, Lynch RE. Hong Kong influenza: The epidemiologic features of a high school family study analyzed and compared with a similar study during the 1957Asian influenza epidemic. *American Journal of Epidemiology* 1970;92(4):520.
77. Miller E, Hoschler K, Hardelid P, Stanford E, Andrews N, Zambon M. Incidence of 2009 pandemic influenza A H1N1 infection in England: a cross-sectional serological study. *Lancet* 2010;375(9720):1100-8.
78. Lowen AC, Mubareka S, Steel J, Palese P. Influenza Virus Transmission Is Dependent on Relative Humidity and Temperature. *PLoS Pathog* 2007;3(10):e151.
79. Shaman J, Goldstein E, Lipsitch M. Absolute humidity and pandemic versus epidemic influenza. *Am J Epidemiol* 2011;173(2):127-35.
80. Shaman J, Kohn M. Absolute humidity modulates influenza survival, transmission, and seasonality. *Proc Natl Acad Sci U S A* 2009;106(9):3243-8.
81. Shaman J, Pitzer VE, Viboud C, Grenfell BT, Lipsitch M. Absolute humidity and the seasonal onset of influenza in the continental United States. *PLoS Biol* 2010;8(2):e1000316.
82. Eames KT, Tilston NL, Brooks-Pollock E, Edmunds WJ. Measured Dynamic Social Contact Patterns Explain the Spread of H1N1v Influenza. *PLoS Comput Biol* 2012;8(3):e1002425.
83. Uchida M, Tsukahara T, Kaneko M, Washizuka S, Kawa S. Swine-origin influenza a outbreak 2009 at Shinshu University, Japan. *BMC Public Health* 2011;11:79.

**Table 1:** Features of the studies identified. Studies may present more than one dataset and so appear in more than one row of each section.

| | | Number of studies |
|---|---|---|
| | ***Total studies*** | ***79*** |
| Type of outbreak | Seasonal | 22 |
| | 1918 pandemic | 7 |
| | 1968 pandemic | 1 |
| | 2009 pandemic | 49 |
| Setting | Europe | 22 |
| | North America | 22 |
| | Central America | 5 |
| | South America | 3 |
| | Asia | 20 |
| | Africa | 1 |
| | Australasia | 6 |
| Data provided on[1]: | Children only | 25 |
| | General population | 29 |
| | School pupils and staff | 5 |
| | Children and other specified groups separately | 22 |
| Reason for closure | High student absenteeism | 3 |
| | High staff absenteeism | 1 |
| | High student and staff absenteeism | 1 |
| | Other reactive closure[2] | 31 |
| | Pro-active | 7 |
| | Planned holiday | 38 |
| | Other[3] | 3 |
| | Unclear | 3 |
| Period of closure | Continuous | 67 |
| | Intermittent | 8 |
| | Variable[4] | 3 |
| | Not stated | 1 |
| Other interventions in place[5] | None | 20 |
| | Antivirals | 33 |
| | Other social distancing | 24 |
| | Vaccination | 8 |
| | Other | 20 |
| Timing of closure | Before peak | 21 |
| | Same day / week as peak | 9 |
| | After peak | 36 |
| | Variable[4] | 8 |
| | Unclear | 8 |
| Duration of closure[6] | <7 days | 8 |
| | 7-13 days | 33 |
| | 14-20 days | 19 |
| | ≥21 days | 17 |
| | Variable[4] | 6 |
| | Not stated | 2 |

[1] Each study may present more than one data source

[2] Closure in response to outbreak, not stated as being for operational reasons

[3] Teachers' strike (2 studies) or response to SARS outbreak (1 study)

[4] Studies of multiple US cities during the 1918 pandemic or multiple countries in 2009

[5] Described in the included paper or related papers; excludes normal levels of vaccine and antiviral usage in seasonal datasets.

[6] Each study may present more than one dataset for which the durations of closure differed

***Figure legends***

**Figure 1:** Identification of epidemiological studies of the effects of school closure on influenza outbreaks

**Figure 2:** Peak cumulative attack rates recorded in the identified studies. Case definitions varied between studies (see Appendix); only studies which included a denominator are shown. Studies which reported peak prevalence of absenteeism are denoted by an asterisk. See Appendix for full details of datasets. Abbreviations: BC, British Colombia; IL, Illinois; CT, Connecticut; NC, North Carolina; UK, United Kingdom; KI, Kelleys Island. All pandemic data are from 2009 except for Kelleys Island.

**Figure 3:** Normalised peak attack rates (estimated as peak attack rate / median attack rate) recorded in the identified studies; one study with an estimate normalised peak of 128 is excluded for clarity [83]. Case definitions varied between studies (see Appendix). Studies which reported peak prevalence of absenteeism are denoted by an asterisk. Abbreviations: HK, Hong Kong; IL, Illinois; SARI, severe acute respiratory infection; NC, North Carolina; UK, United Kingdom; KI, Kelleys Island.

**Box 1: Information extracted from eligible studies (where presented)**

Study design

Study population / setting (including size of population)

Nature of school closure (e.g. school holiday, response to outbreak)

Duration of closure and number of schools affected

Timing of closure in relation to influenza circulation

Outcome measure(s) examined (e.g. clinical ILI, virologically confirmed influenza)

Association between school closure and outcome

Epidemic curve (transcribed from graphs or figures); used to derive peak, cumulative and median attack rates

Normalised peak attack rate (= peak attack rate / median attack rate)

School closures and influenza: systematic review of epidemiological studies

Charlotte Jackson[1], Emilia Vynnycky[2], Jeremy Hawker[3], Babatunde Olowokure[3], Punam Mangtani[1]

[1] London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK; [2] Health Protection Agency, Colindale, London NW9 5EQ, UK; [3] Health Protection Agency, 5 St Philips Place, Birmingham B3 2PW, UK

Corresponding author: Charlotte Jackson, Room 113, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT.

Email: charlotte.jackson@lshtm.ac.uk

Tel: +44 (0) 207 927 2209

Word count: ~~3540~~3999

*Abstract*

Objective: To review the effects of school closures on pandemic and seasonal influenza outbreaks.

Design: Systematic review.

Data sources: Medline and Embase, reference lists of identified articles, hand searches of key journals, and additional papers from the authors' collections.

Study selection: Studies were included if they reported on a seasonal or pandemic influenza outbreak coinciding with a planned or unplanned school closure.

Results: Of 2579 papers identified through Medline and Embase, 65 were eligible for inclusion in the review along with ~~13~~ 14 identified from other sources. Influenza incidence frequently declined after school closure. The effect was sometimes reversed when schools reopened, supporting a causal role for school closure in reducing incidence. Any benefits associated with school closure appeared to be greatest amongst school-aged children. However, as schools often closed late in the outbreak or other interventions were used concurrently, it was sometimes unclear how much school closure contributed to the reductions in incidence.

Conclusions: School closures appear to have the potential to reduce influenza transmission, but the heterogeneity in the data available means that the optimum strategy (e.g. the ideal length and timing of closure) remains unclear.

***Introduction***

During the 2009 influenza pandemic, schools were closed in many settings in efforts to reduce transmission. The World Health Organization does not specifically recommend or discourage school closures during an influenza pandemic, as their potential benefits and harms may be context-specific [1], but has suggested that they be considered as part of a mitigation strategy [2]. Their effects on transmission ~~are~~, however, ~~still~~ remain poorly understood [3 4]. Closures may be ~~either~~ pro-active (occurring before transmission is established in the school) or reactive (a response to a school-based outbreak), and may involve closure of whole school(s) or dismissal of individual classes [4].

A review of the evidence available before the 2009 pandemic concluded that school closures may be beneficial, depending on characteristics such as age-specific attack rates [4]. Here, we review epidemiological studies to assess the effects of school closures on transmission and incidence of seasonal and pandemic influenza, updating and extending previous reviews [2 4] to include data from the 2009 pandemic.

***Methods***

*Search strategy and selection criteria*

Medline and Embase were searched in January 2012, without language restrictions, for relevant papers published by the end of 2011 (see Appendix for search strategy). *Eurosurveillance* (23 April 2009 to 15 December 2011), *Morbidity and Mortality Weekly Report* (24 April 2009 to 23 December 2011) and *Emerging Infectious Diseases* (April 2009 to December 2011) were hand~~-~~searched. Results were ~~also~~ supplemented with papers from the reference lists of the articles identified, and papers from the reviewers' collections. An additional ~~search of~~ Pubmed search (for the words "influenza" and "school") was used to identify relevant papers published during October – December 2011 ~~which were~~but not yet listed in Medline or Embase.

Studies were included if they described one or more influenza outbreaks during which schools were initially open and subsequently closed ~~on specified dates~~, with or without other interventions. If papers presented several measures of influenza activity, the most specific data were extracted (e.g. data on laboratory-confirmed influenza were extracted in preference to all-cause school absenteeism). Studies which used modelling techniques to assess how school closure affected transmission based on real epidemic curves were eligible; however, predictive modelling studies exploring how school closure might affect a hypothetical outbreak were excluded. English translations (where available) of the titles and abstracts of papers written in other languages were screened, but these papers were not eligible for inclusion. Studies of outbreaks which started during school closure were excluded.

Abstracts and full text were screened initially by one reviewer and by a second reviewer if necessary. Box 1 summarises the information extracted from the studies. Where possible, epidemic curves were plotted by transcribing daily or weekly data from figures or tables.

*Data analysis*

We summarised the data graphically and descriptively. We plotted the peak and cumulative attack rates (and 95% confidence intervals, calculated using standard methods for calculating CIs for proportions) for each study that provided an appropriate denominator. We calculated the normalised peak (peak AR / median AR) for datasets with a median AR greater than zero, to adjust approximately for differences in case definitions (this approach has been used elsewhere to adjust for intercity differences in case fatality proportions [5]). These estimates were stratified by the timing of closure, i.e. whether schools closed before, coincident with, or after the peak.

***Results***

Of 2579 papers identified through Medline and Embase, 430 were reviewed in full. 65 of these studies were included in the review, along with ~~13~~ 14 additional papers (Figure 1; the supplementary PubMed search yielded no further eligible articles). ~~78~~ 79 papers were thus included in the review: ~~22~~ 23 for seasonal and 56 for pandemic influenza (49, one, and ~~six~~ seven from the 2009, 1968 and 1918 pandemics, respectively). Details of the studies are given in Table 1 and Supplementary Tables 1 and 2.

*Description of the epidemics*

19 and 41 epidemic curves were available on seasonal and pandemic influenza, respectively (Supplementary Figures 1 and 2). School closure was often followed by a reduction in incidence, in children specifically or ~~in~~ the general population. However, closure often occurred late in the outbreaks (Table 1), and it is unclear whether it influenced the decline.

The cumulative and peak ARs varied widely for seasonal and pandemic influenza (Figure 2). Normalised peaks partly account for differences in case definitions between studies, but also varied considerably (Figure 3). There was no clear pattern in the cumulative, peak or normalised peak ARs plotted by timing of closure in relation to the peak. Relatively few schools closed before the peak (Figures 2 and 3); of those that did, two also reopened before the peak [6,7]. However, early introduction of non-pharmaceutical interventions (NPIs), which often included school closures, in US cities during the 1918 ~~influenza~~ pandemic has been found to be associated with a reduction in mortality [5 8 9]. In Connecticut in 1918, three cities which closed schools experienced higher mortality rates than two which did not [10].

*Age-specific effects of school closure*

The available age-specific data suggested that any benefits associated with school closure were greatest amongst school-aged children [11-25]. In New Zealand during the 2009 pandemic, the age-standardised proportion of confirmed cases in 5-19 year-olds fell during the winter holiday and increased when schools reopened [19]; a slight increase in ILI consultation rates when schools reopened was confined to 5-14 year-olds [14]. Similar relationships between school closure and the ratio of the number of H1N1 infections in 5-20 year-olds to that in other age groups were reported for Mexico [23] and Peru [26]. During the 1967-68 influenza season in Great Britain, GP consultation rates for ILI amongst 5-14 year-olds declined during the Christmas holiday and increased when schools reopened; this effect was less clear in other age groups [17].

Winter holidays in Israel were associated with a reduction in the ratio between the number of clinic visits for influenza and those for non-respiratory complaints, in 6-12 year-olds, in three of five seasonal influenza periods studied [15]. In one season, this ratio was also reduced in adults, and in another it was reduced for adults not living with 6-12 year-olds. When a two-week teachers' strike coincided with an influenza outbreak in January 2000, closing 80% of elementary schools nationwide, this ratio decreased by 15% for 6-12 year-olds (95% CI 6-23%), but not for older individuals. As the authors note, children comprise a high proportion (34%) of the Israeli population, which may contribute to any apparent benefit of closing schools in Israel [27].

Similar data from four influenza seasons in Arizona are less consistent, partly because school closure rarely coincided with elevated influenza activity [18]. During all four seasons, rates of laboratory-confirmed influenza in school-aged children were similar during the two week winter holiday and the preceding two weeks. In two seasons this rate increased in the two weeks after schools reopened; in one other season, it was significantly lower on reopening than during closure [18]. In comparison, rates in adults and pre-school-aged children increased successively (though not always significantly) across the three two-week periods in three of the seasons [18].

Three studies which fitted transmission models to surveillance data also concluded that school closures mainly benefit children [12 13]. Analyses of French seasonal ILI data [13] and ILI data from London during the 2009 pandemic [22] estimated that school holidays did not affect adults' contact patterns; similarly, reductions in transmission following school closures in Hong Kong in 2009 occurred primarily amongst children [12].

However, two studies of the 2009 pandemic suggested that school closure affected incidence in adults. One of these studies estimated the age-specific number of ILI cases due to pandemic H1N1 in England; in most age groups, these estimated case numbers decreased during the summer holiday and increased when schools reopened [25]. In Vojvodina, Serbia, incidence decreased amongst 5-14 and 15-64 year ~~-~~olds during a one-week school closure [28].

*Reversibility of effects*

Incidence sometimes rebounded when schools reopened, suggesting that school closure contributed to reducing incidence in some settings. For example, during the 2009 pandemic in England, the estimated weekly number of infections declined during the school summer holiday; a second wave occurred when schools reopened (Supplementary Figure 2) [22 29]. Similar reversibility appeared in ILI consultation rates in Vojvodina in 2009 [28]. Datasets from the 2009 pandemic in Mexico [23 30 31] also suggested an increase in incidence after schools reopened (Supplementary Figure 2). Analyses of NPIs (usually including school closures) during the 1918 pandemic found that, in the cities studied, second waves occurred only after NPIs were lifted [5 8].

In the Israeli data regarding seasonal influenza and the teachers' strike, the number of physician visits for acute respiratory illness was 42% lower during the closure compared to the previous two weeks; incidence increased after the strike [27]. During the 1999-2000 influenza season in Japan, the increase in incidence appeared to slow during the two week winter holiday and accelerated when schools reopened [7]. Similarly, in Beijing in 2009, the cumulative incidence of laboratory-confirmed H1N1 influenza increased more markedly before and after a national school holiday than during the break [32].

*Changes in transmission patterns from modelling analyses of epidemic data*

Several studies have fitted transmission models to observed epidemic data to estimate the reduction in contact rates associated with school closure. School holidays were estimated to reduce transmission of seasonal influenza amongst children by a median of 24% (range 20-29%), based on rates of ILI in France from 1985 to 2006, corresponding to a 16-18% reduction in total case numbers [13]. During the 2009 pandemic in London, contact amongst 5-14 year-olds was reduced by an estimated 72% during the six-week summer holiday; the corresponding reduction during one-week half term holidays was 48% [22]. In US cities in 1918, changes in mortality were attributed to a combination of formal interventions (including school closure) and spontaneous social distancing [8]. In Sydney in 1918, formal and spontaneous social distancing together were estimated to have reduced contact rates by up to 38% [33]. Based on influenza incidence data from the 2009 pandemic in Mexico City, school closure together with other interventions appeared to reduce the population contact rate by 23% [31]. A subsequent analysis of national data from Mexico estimated that the contact rate was reduced by 30% during the intervention period [23].

In Hong Kong (also during the 2009 pandemic), closing primary schools, kindergartens, and childcare centres pro-actively, together with affected secondary schools, was estimated to reduce transmission by 70% amongst children and 25% in the population overall [12]. The same study estimated the effective reproduction number ($R_n$, the average number of secondary infectious persons generated by a single infectious person in a given population) as 1·7 before school closure, 1·5 during school closure, and 1·1 during the subsequent school holidays [12]. Daily estimates of $R_n$ in Hong Kong in 2009 (based on a longer time series) also suggested a decline during school closure and a slight increase following reopening [34].

Modelling techniques have also been used to estimate daily values of $R_n$ during a seasonal influenza outbreak in Hong Kong [35] and the 2009 pandemic in Mexico City [23 31] and New Zealand [19]. The Hong Kong analysis for seasonal influenza suggested that $R_n$ was not substantially affected by school closure, perhaps because closure occurred late in the outbreak when $R_n$ was already below one [35]. In Mexico City [31] and New Zealand, $R_n$ was declining before schools closed and continued to decrease during closure; in New Zealand, $R_n$ increased briefly but not substantially when schools reopened [19]. Analysis of a further outbreak in the USA detected no clear effect of school closure on transmission, which was attributed to the late timing of closure [20].

Modelling analyses of the spatiotemporal spread of pandemic H1N1 in Europe in 2009 were able to reproduce observed incidence patterns only when contact rates were allowed to change specifically during each country's school holidays (holidays were assumed to eliminate transmission in schools and increase community transmission by a factor of 1.4) [36]. In all countries, holidays were estimated to delay the peak compared to a hypothetical situation without school closure. In contrast, regression analysis of estimates of $R_n$ in 12 European countries found no evidence of an effect of school holidays on transmission in the nine countries in which school holidays coincided with the study period [37]. The authors proposed that this apparent lack of effect might result from changes in reporting, stochastic effects early in the outbreaks, and the fact that in some countries (including England), school holidays occurred outside the study period.

*Different school closure strategies*

In some outbreaks, individual schools were closed; in others, school closure was more widespread (Supplementary Tables 1 and 2). The effects of these different strategies could not be compared, due to both late implementation and differences between the studies in other factors (such as the duration of closure).

Analyses of the 1918 pandemic in US cities found that the duration of NPIs was negatively associated with the total excess death rate [9]. In the datasets reviewed here, closures longer than two weeks were associated with reduced incidence or transmission in several studies of seasonal [38] and pandemic [12 29] influenza, but not in others [11 39]. Two studies which suggested reasonably strong evidence of an effect of school closure (from France and Israel) reported on closures lasting two weeks [13 27]. Studies in Japan [7] and England and Wales [17] also suggested possible effects of two-week closures on seasonal influenza. However, closures of this length did not always appear to reduce transmission [35]. Shorter closures, e.g. of 1-2 weeks, may sometimes have contributed to reductions in transmission [22 29 31 32 40], but often had no obvious effect [41-44]. In London, contacts between children were reduced more dramatically during a six-week holiday than during one-week breaks, but this may reflect different behaviour during the different holidays [22].

*Use of multiple interventions*

In most of the pandemic influenza studies, other interventions were implemented alongside school closure and may have contributed to any reduction in incidence. In 2009, antiviral treatment and / or prophylaxis was commonly used in the studies identified [12 14 19 20 39 40 42 45-57]. Public places were sometimes closed and / or large gatherings were discouraged or restricted [16 30 31 58]. Some datasets from the 2009 pandemic included vaccination against the pandemic strain, although this was usually only available late in the study period so would not affect the included incidence data [29 32 57 59]. In 1918, school closures were often combined with other social distancing measures [5 8 9 33]; the only study included from the 1968 pandemic was a vaccine trial [60]. Of the few pandemic studies which mentioned no additional interventions, one suggested an effect of school closures: in Israel in 2009, three waves of infection corresponded to the planned closure and reopening of schools [61]. In the England and Wales data for the 2009 pandemic, other interventions (vaccination and antivirals) were used to only a limited extent; incidence still clearly declined during the school summer holiday and increased afterwards [29].

Some studies of seasonal influenza mentioned additional interventions (e.g. vaccination [62-64], prophylactic amantadine [65], hygiene promotion [38 41 66], closure of public places [38], and advice

to avoid large gatherings [44]). However, some studies without additional interventions showed reductions in incidence and / or transmission during school closure [13,27].

***Discussion***

This systematic review of the effects of school closures on influenza outbreaks extends previous reviews [2,4] to include published experiences from the 2009 pandemic. The results suggest that school closure can reduce transmission of pandemic [12] and seasonal [13,27] influenza amongst schoolchildren. Many datasets, however, show no clear effect of school closure. As noted by some authors [20,43,44], this may sometimes have been because schools shut late in the outbreak (often close to or after the peak).

In some studies, incidence increased when schools reopened [5,7,8,14,22,27,29,31]. This apparent reversibility provides evidence that school closure can cause reductions in influenza incidence. In two of the studies of seasonal influenza which showed reversibility [7,27], no additional interventions (beyond usual seasonal interventions) were used. In many other datasets, multiple interventions were used, so the specific effects of school closures are difficult to isolate.

~~[2,4]~~In 2009, several countries closed schools whilst in others, planned holidays coincided with outbreaks. Several datasets from this pandemic strengthen support for school closure as an intervention; however, others illustrate that benefits are not guaranteed and that timely closure may be challenging. The sensitivity of the 2009 pandemic to school closures probably reflects the age-specific attack rates, which were higher in children than adults; outbreaks in which children are less affected might be less sensitive to school closure.

Studies presenting age-stratified data suggested that the effects of school closure on transmission were greater amongst children than adults. Few studies stratified children further, e.g. into primary and secondary school students. Older children might socialise more than younger children during school closures, so closing primary schools may have a greater effect on transmission than closing secondary schools (e.g. in Hong Kong in 2009, primary schools were closed pro-actively whilst secondary schools closed if cases occurred amongst their students [12]).

The long term effects of closing schools are unclear, as relatively few of the studies presented substantial data after schools reopened. For example, school closure could result in multiple peaks, potentially involving more cases than would otherwise have occurred [8]. However, a study published since this review was conducted estimated that case numbers in Alberta, Canada, could have been up to twice as high as those seen if schools had not closed for planned holidays [67]. It is difficult to compare reactive versus pro-active closures, different durations of closure, and local versus national closures as studies typically differed in several respects. Age-specific data suggest that the effects of school closure are greatest among school-aged children [12-15 17 22].

Some studies have concluded that reopening schools after holiday periods can accelerate epidemic growth (e.g. during the 1957 [68 69] and 2009 [70] pandemics). These studies were beyond the scope of this review of the effects of closing schools after outbreaks have started, but they suggest that extending school holidays might delay the spread of an epidemic beginning during a break.

Results from analyses of seasonal influenza may not be directly applicable to a pandemic. Schools were often closed for planned holidays rather than in response to the outbreaks; contact patterns may differ between reactive school closures [71] and holidays [72]. Extrapolating from previous pandemics may also be problematic. Modelling studies [73-75] have predicted that school closures will have the greatest effects if transmission occurs mainly amongst children. The importance of children in transmission has varied between pandemics [76]; in 2009, attack rates were higher in children than in adults, probably because of pre-existing immunity in older individuals [77]. Viral virulence will also influence individuals' responses to school closure and other interventions, e.g. spontaneous social distancing during a mild pandemic may be less dramatic than occurred in 1918. Changes in household size, contact patterns, children's behaviour and school systems since 1918, 1957 and 1968 may also limit the generalisability of experiences from these pandemics. As noted in a study of the 1918 pandemic in Connecticut, reverse causality may occur when comparing rates in cities which closed schools to those in cities which did not, if closure was a response to a particularly severe local outbreak [10].

One limitation of the datasets is that ascertainment may have changed during the outbreaks, due to changes in surveillance and care-seeking behaviour. Increases in ascertainment during an outbreak could obscure any reductions in incidence during school closures (e.g. in one study, enhanced surveillance began the day the school closed [56]). Conversely, the proportion of patients who undergo virological testing may be reduced late in an outbreak, and in some settings (e.g. New Zealand [14]) patients with ILI were discouraged from consulting GPs during the 2009 pandemic. The estimated proportion of influenza cases that were reported in Hong Kong declined to ~5% of its original value during the move from containment to mitigation during the 2009 pandemic [12]. In England, the introduction of the National Pandemic Flu Service telephone helpline coincided with the school holiday, and was estimated to have reduced the probability of GP consultation for adults with ILI from 16% to 1.8% [22].

Case definitions may not always have been well-suited to detecting any effect of school closure. For example, school absenteeism is a relatively non-specific measure, whilst laboratory specimens frequently represent severe infections (e.g. in the elderly, who may have little contact with children and therefore be relatively unaffected by school closure).

Influenza transmission is influenced by factors besides contact in schools, including temperature and absolute humidity (AH) [78-81]. Two studies which assessed the role of AH during the 2009 pandemic did not find strong evidence that it affected transmission [24 37]. The two waves seen in the UK in 2009 could be explained by changes in contact patterns during school holidays [29 82]. In a modelling study of data from Alberta, Canada, the best-fitting model included effects of temperature and school holidays on transmission, and predicted that if schools had not closed, the outbreak would have been restricted by temperature effects but would still have been 2.1 times larger than was observed in the province as a whole (1.38 and 1.54 times in the cities of Calgary and Edmonton, respectively) [67]. A study of the interplay between school calendars, AH and population susceptibility in enhancing influenza transmission concluded that high AH may prevent influenza outbreaks [79]. However, if a sufficiently high proportion of the population is susceptible, outbreaks can occur even when AH is high; the opening of schools may enhance transmission [79]. Taken together, these studies suggest that contact in schools is not the only determinant of influenza transmission, but it is one influential (and modifiable) factor.

Previous studies have attempted to estimate the effects of public health interventions using transmission models [8 12 20 31]. The development of such models is complicated for the datasets reviewed here, and would not necessarily have provided conclusive insight into the impact of school closures. For example, many factors are unknown and would need to be estimated or assumed for each dataset, such as the basic reproduction number, proportion of infections that were reported, the effect of other interventions, and the proportion of individuals who were immune at the start of the outbreak.

The review was limited to published studies, which could potentially introduce publication bias. However, many of the studies identified did not aim to evaluate the effects of school closure on transmission, so publication bias appears unlikely. This is supported by the apparent lack of an effect of school closure in many of the studies (including some of those which did specifically assess school closure as an intervention). Foreign language papers were excluded, but in most cases it was clear from the title and / or abstract (available in English) that the papers were not relevant to this review.

***Conclusions***

The available data suggest that school closures can potentially reduce transmission during an influenza outbreak, even in the absence of other interventions, although the optimal school closure strategy is unclear. The effect of school closures is larger for school-aged children than for other age groups, although there is some evidence that incidence in adults might also be reduced. During a future pandemic (or seasonal outbreaks during which schools are closed), it will be important to collect incidence data using systematic ascertainment and a consistent case definition, before, during and after school closure, to assess the effects of school closures on transmission. Analysis of comparable data from multiple outbreaks may help to overcome some of the problems with comparability and ascertainment discussed above, and clarify which features determine the effectiveness of school closures. Although timely school closures may reduce transmission, other implications of school closure (e.g. ethical and economic considerations) [4], and viral properties such as virulence, must also be considered in policy decisions, and may depend on the local context [1].

***Summary***

*Article focus*

- This systematic review assesses the effects of school closures on transmission of influenza, including data from the recent 2009 pandemic as well as from previous pandemics and seasonal outbreaks.

*Key messages*

- The available data suggest that school closure can be a useful intervention during influenza outbreaks, with the greatest benefits occurring amongst school-aged children.

*Strengths and limitations*

- We have reviewed an extensive body of literature on the effects of school closure on the incidence and transmission of influenza.
- The optimum timing and duration of closure are unclear because studies often differed in several respects, or used other interventions in addition to school closure.

*Acknowledgements*

This paper developed from a review commissioned by the UK Health Protection Agency as part of its pandemic influenza programme. We thank Nadia Inglis, Angus Nicoll and two anonymous members of the HPA's Influenza and Respiratory Virus Programme Board for helpful comments on the review. We also thank staff at the LSHTM library for assistance in locating papers.

*Funding*

This work was partially funded by the Health Protection Agency; C.J. was supported by a Research Training Fellowship from the National Institute for Health Research.

*Role of the funding source*

NIHR had no role in the design and conduct of the study; collection, analysis or interpretation of data; writing of the report; or the decision to submit the article for publication. The HPA commissioned the research.

*Access to data*

All authors had full access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

*Data sharing*

No additional data available.

*Competing interest statement*

All authors have completed the Unified Competing Interest form at http://www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: funding from NIHR and HPA; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

*Statement of authors' roles*

B.O and J.H. had the initial idea. P.M., C.J. and E.V. developed the research questions and study design. C.J. carried out the literature review and P.M. assessed any doubtful papers. C.J., P.M. and E.V. analysed data. C.J., P.M. and E.V. wrote the paper. J.H. commented on outputs and contributed to the final draft. J.H. and B.O. contributed to the final draft.

*Ethical approval*

Not required.

***References***


1. World Health Organization. Reducing transmission of pandemic (H1N1) 2009 in school settings. A framework for national and local planning and response, 2009.
2. Bell DM, World Health Organization Writing Group. Non-pharmaceutical interventions for pandemic influenza, national and community measures. *Emerg Infect Dis* 2006;12(1):88-94.
3. Aledort JE, Lurie N, Wasserman J, Bozzette SA. Non-pharmaceutical public health interventions for pandemic influenza: an evaluation of the evidence base. *BMC Public Health* 2007;7:208.
4. Cauchemez S, Ferguson NM, Wachtel C, Tegnell A, Saour G, Duncan B, et al. Closure of schools during an influenza pandemic. *The Lancet Infectious Diseases* 2009;9(8):473-81.
5. Hatchett RJ, Mecher CE, Lipsitch M. Public health interventions and epidemic intensity during the 1918 influenza pandemic. *Proc Natl Acad Sci U S A* 2007;104(18):7582-7.
6. Olson JG. School absenteeism during an outbread of B/Hong Kong/5/72-like influenze virus in Taipei, Taiwan. *Southeast Asian J Trop Med Public Health* 1980;11(4):429-34.
7. Fujii H, Takahashi H, Ohyama T, Hattori K, Suzuki S. Evaluation of the school health surveillance system for influenza, Tokyo, 1999-2000. *Japanese Journal of Infectious Diseases* 2002;55(3):97-98.
8. Bootsma MC, Ferguson NM. The effect of public health measures on the 1918 influenza pandemic in U.S. cities. *Proc Natl Acad Sci U S A* 2007;104(18):7588-93.
9. Markel H, Lipman HB, Navarro JA, Sloan A, Michalsen JR, Stern AM, et al. Nonpharmaceutical interventions implemented by US cities during the 1918-1919 influenza pandemic.[Erratum appears in JAMA. 2007 Nov 21;298(19):2264]. *Jama* 2007;298(6):644-54.
10. Winslow C-EA, Rogers JF. Statistics of the 1918 Epidemic of Influenza in Connecticut: With a consideration of the factors which influenced the prevalence of this disease in various communities *J Infect Dis* 1920;26(3):185-216.
11. Armstrong C, Hopkins R. An epidemiological study of the 1920 epidemic of influenza in an isolated rural community. *Public Health Reports* 1921;36(29):1671-702.
12. Wu JT, Cowling BJ, Lau EH, Ip DK, Ho LM, Tsang T, et al. School closure and mitigation of pandemic (H1N1) 2009, Hong Kong. *Emerg Infect Dis* 2010;16(3):538-41.
13. Cauchemez S, Valleron A-J, Boelle P-Y, Flahault A, Ferguson NM. Estimating the impact of school closure on influenza transmission from Sentinel data. *Nature* 2008;452(7188):750-4.
14. Baker MG, Wilson N, Huang QS, Paine S, Lopez L, Bandaranayake D, et al. Pandemic influenza A(H1N1)v in New Zealand: the experience from April to August 2009. *Euro Surveill* 2009;14(34).
15. Heymann AD, Hoch I, Valinsky L, Kokia E, Steinberg DM. School closure may be effective in reducing transmission of respiratory viruses in the community. *Epidemiol Infect* 2009;137(10):1369-76.
16. Tinoco Y, Razuri H, Ortiz EJ, Gomez J, Widdowson MA, Uyeki T, et al. Preliminary population-based epidemiological and clinical data on 2009 pandemic H1N1 influenza A (pH1N1) from Lima, Peru. *Influenza Other Respi Viruses* 2009;3(6):253-6.
17. Miller DL, Lee JA. Influenza in Britain 1967-68. *Journal of Hygiene* 1969;67:559-72.

18. Wheeler CC, Erhart LM, Jehn ML. Effect of school closure on the incidence of influenza among school-age children in Arizona. *Public Health Rep* 2010;125(6):851-9.
19. Paine S, Mercer GN, Kelly PM, Bandaranayake D, Baker MG, Huang QS, et al. Transmissibility of 2009 pandemic influenza A(H1N1) in New Zealand: effective reproduction number and influence of age, ethnicity and importations. *Euro Surveill* 2010;15(24).
20. Cauchemez S, Bhattarai A, Marchbanks TL, Fagan RP, Ostroff S, Ferguson NM, et al. Role of social networks in shaping disease transmission during a community outbreak of 2009 H1N1 pandemic influenza. *Proc Natl Acad Sci U S A* 2011;108(7):2825-30.
21. Marchbanks TL, Bhattarai A, Fagan RP, Ostroff S, Sodha SV, Moll ME, et al. An outbreak of 2009 pandemic influenza A (H1N1) virus infection in an elementary school in Pennsylvania. *Clin Infect Dis* 2011;52 Suppl 1:S154-60.
22. Birrell PJ, Ketsetzis G, Gay NJ, Cooper BS, Presanis AM, Harris RJ, et al. Bayesian modeling to unmask and predict influenza A/H1N1pdm dynamics in London. *Proceedings of the National Academy of Sciences of the United States of America* 2011;108(45):18238-43.
23. Chowell G, Echevarria-Zuno S, Viboud C, Simonsen L, Tamerius J, Miller MA, et al. Characterizing the epidemiology of the 2009 influenza A/H1N1 pandemic in Mexico. *PLoS Med* 2011;8(5):e1000436.
24. Chowell G, Viboud C, Munayco CV, Gomez J, Simonsen L, Miller MA, et al. Spatial and temporal characteristics of the 2009 A/H1N1 influenza pandemic in Peru. *PLoS ONE* 2011;6(6):e21287.
25. Evans B, Charlett A, Powers C, McLean E, Zhao H, Bermingham A, et al. Has estimation of numbers of cases of pandemic influenza H1N1 in England in 2009 provided a useful measure of the occurrence of disease? *Influenza and other Respiratory Viruses* 2011;5(6):e504-e12.
26. Munayco CV, Gomez J, Laguna-Torres VA, Arrasco J, Kochel TJ, Fiestas V, et al. Epidemiological and transmissibility analysis of influenza A(H1N1)v in a southern hemisphere setting: Peru. *Euro surveillance : bulletin europeen sur les maladies transmissibles = European communicable disease bulletin* 2009;14(32).
27. Heymann A, Chodick G, Reichman B, Kokia E, Laufer J. Influence of school closure on the incidence of viral respiratory diseases among children and on health care utilization. *Pediatr Infect Dis J* 2004;23(7):675-7.
28. Petrovic V, Seguljev Z, Cosic G, Ristic M, Nedeljkovic J, Dragnic N, et al. Overview of the winter wave of 2009 pandemic influenza A(H1N1)v in Vojvodina, Serbia. *Croatian Medical Journal* 2011;52(2):141-50.
29. Baguelin M, Hoek AJV, Jit M, Flasche S, White PJ, Edmunds WJ. Vaccination against pandemic influenza A/H1N1v in England: A real-time economic evaluation. *Vaccine* 2010;28(12):2370-84.
30. Echevarria-Zuno S, Mejia-Arangure JM, Mar-Obeso AJ, Grajales-Muniz C, Robles-Perez E, Gonzalez-Leon M, et al. Infection and death from influenza A H1N1 virus in Mexico: a retrospective analysis. *Lancet* 2009.
31. Cruz-Pacheco G, Duran L, Esteva L, Minzoni A, Lopez-Cervantes M, Panayotaros P, et al. Modelling of the influenza A(H1N1)v outbreak in Mexico City, April-May 2009, with control sanitary measures. *Euro Surveill* 2009;14(26).
32. Wu J, Xu F, Lu L, Lu M, Miao L, Gao T, et al. Safety and effectiveness of a 2009 H1N1 vaccine in Beijing. *New England Journal of Medicine* 2010;363(25):2416-23.
33. Caley P, Philp DJ, McCracken K. Quantifying social distancing arising from pandemic influenza. *Journal of the Royal Society Interface* 2008;5(23):631-9.

34. Cowling BJ, Lau MSY, Ho LM, Chuang SK, Tsang T, Liu SH, et al. The effective reproduction number of pandemic influenza: Prospective estimation. *Epidemiology* 2010;21(6):842-46.
35. Cowling BJ, Lau EHY, Lam CLH, Cheng CKY, Kovar J, Chan KH, et al. Effects of school closures, 2008 winter influenza season, Hong Kong. *Emerg Infect Dis* 2008;14(10):1660-2.
36. Merler S, Ajelli M, Pugliese A, Ferguson NM. Determinants of the spatiotemporal dynamics of the 2009 H1N1 pandemic in europe: Implications for real-time modelling. *PLoS Computational Biology* 2011;7(9).
37. Flasche S, Hens N, Boëlle P-Y, Mossong J, van Ballegooijen WM, Nunes B, et al. Different transmission patterns in the early stages of the influenza A(H1N1)v pandemic: A comparative analysis of 12 European countries. *Epidemics* 2011;3(2):125-33.
38. Lo JY, Tsang TH, Leung YH, Yeung EY, Wu T, Lim WW. Respiratory infections during SARS outbreak, Hong Kong, 2003. *Emerg Infect Dis* 2005;11(11):1738-41.
39. Gomez J, Munayco C, Arrasco J, Suarez L, Laguna-Torres V, Aguilar P, et al. Pandemic influenza in a southern hemisphere setting: the experience in Peru from May to September, 2009. *Euro Surveill* 2009;14(42).
40. Kawaguchi R, Miyazono M, Noda T, Takayama Y, Sasai Y, Iso H. Influenza (H1N1) 2009 outbreak and school closure, Osaka Prefecture, Japan. *Emerg Infect Dis* 2009;15(10):1685.
41. Danis K, Fitzgerald M, Connell J, Conlon M, Murphy PG. Lessons from a pre-season influenza outbreak in a day school. *Commun Dis Public Health* 2004;7(3):179-83.
42. Calatayud L, Kurkela S, Neave PE, Brock A, Perkins S, Zuckerman M, et al. Pandemic (H1N1) 2009 virus outbreak in a school in London, April-May 2009: an observational study. *Epidemiol Infect* 2010;138(2):183-91.
43. Rodriguez CV, Rietberg K, Baer A, Kwan-Gett T, Duchin J. Association between school closure and subsequent absenteeism during a seasonal influenza epidemic. *Epidemiology* 2009;20(6):787-92.
44. Johnson AJ, Moore ZS, Edelson PJ, Kinnane L, Davies M, Shay DK, et al. Household responses to school closure resulting from outbreak of influenza B, North Carolina. *Emerg Infect Dis* 2008;14(7):1024-30.
45. Smith A, Coles S, Johnson S, Saldana L, Ihekweazu C, O'Moore E. An outbreak of influenza A(H1N1)v in a boarding school in South East England, May-June 2009. *Euro Surveill* 2009;14(27):9.
46. Effler PV, Carcione D, Giele C, Dowse GK, Goggin L, Mak DB. Household responses to pandemic (H1N1) 2009-related school closures, Perth, Western Australia. *Emerg Infect Dis* 2010;16(2):205-11.
47. Health Protection Agency West Midlands H1N1v Investigation Team. Preliminary descriptive epidemiology of a large school outbreak of influenza A(H1N1)v in the West Midlands, United Kingdom, May 2009. *Euro Surveill* 2009;14(27).
48. Wallensten A, Oliver I, Lewis D, Harrison S. Compliance and side effects of prophylactic oseltamivir treatment in a school in South West England. *Euro Surveill* 2009;14(30):19285.
49. Strong M, Burrows J, Stedman E, Redgrave P. Adverse drug effects following oseltamivir mass treatment and prophylaxis in a school outbreak of 2009 pandemic influenza A(H1N1) in June 2009, Sheffield, United Kingdom. *Euro Surveill* 2010;15(19):pii/19565.

50. Guinard A, Grout L, Durand C, Schwoebel V. Outbreak of influenza A(H1N1)v without travel history in a school in the Toulouse district, France, June 2009. *Euro Surveill* 2009;14(27).
51. France AM, Jackson M, Schrag S, Lynch M, Zimmerman C, Biggerstaff M, et al. Household transmission of 2009 influenza A (H1N1) virus after a school-based outbreak in New York City, April-May 2009. *J Infect Dis* 2010;201(7):984-92.
52. Lessler J, Reich NG, Cummings DAT, New York City Department of H, Mental Hygiene Swine Influenza Investigation T, Nair HP, et al. Outbreak of 2009 pandemic influenza A (H1N1) at a New York City school. *N Engl J Med* 2009;361(27):2628-36.
53. Nishiura H, Castillo-Chavez C, Safan M, Chowell G. Transmission potential of the new influenza A(H1N1) virus and its age-specificity in Japan. *Euro Surveill* 2009;14(22):4.
54. Shimada T, Gu Y, Kamiya H, Komiya N, Odaira F, Sunagawa T, et al. Epidemiology of influenza A(H1N1)v virus infection in Japan, May-June 2009. *Euro Surveill* 2009;14(24).
55. Carrillo-Santisteve P, Renard-Dubois S, Cheron G, Csaszar-Goutchkoff M, Lecuit M, Lortholary O, et al. 2009 pandemic influenza A(H1N1) outbreak in a complex of schools in Paris, France, June 2009. *Euro Surveill* 2010;15(25):24.
56. Huai Y, Lin J, Varma JK, Peng Z, He J, Cheng C, et al. A primary school outbreak of pandemic 2009 influenza A (H1N1) in China. *Influenza other respi* 2010;4(5):259-66.
57. Poggensee G, Gilsdorf A, Buda S, Eckmanns T, Claus H, Altmann D, et al. The first wave of pandemic influenza (H1N1) 2009 in Germany: From initiation to acceleration. *BMC Infectious Diseases* 2010;10(155).
58. Miller JC, Danon L, O'Hagan JJ, Goldstein E, Lajous M, Lipsitch M. Student behavior during a school closure caused by pandemic influenza A/H1N1. *PLoS ONE* 2010;5(5):e10425.
59. Hsueh P-R, Lee P-I, Hsiang Chiu A-W, Yen M-Y. Pandemic (H1N1) 2009 vaccination and class suspensions after outbreaks, Taipei City, Taiwan. *Emerg Infect Dis* 2010;16(8):1309-11.
60. Monto AS, Davenport FM, Napier JA, Francis Jr T. Modification of an outbreak of influenza in tecumseh, michigan by vaccination of schookhildren. *J.Infect.Dis* 1970;122(1-2):328-32.
61. Engelhard D, Bromberg M, Averbuch D, Tenenbaum A, Goldmann D, Kunin M, et al. Increased extent of and risk factors for pandemic (H1N1) 2009 and seasonal infl uenza among children, Israel. *Emerging Infectious Diseases* 2011;17(9):1740-43.
62. Briscoe JH. The protective effect of influenza vaccine in a mixed influenza A and B epidemic in a boys' boarding school. *J R Coll Gen Pract* 1977;27(166):28-31.
63. Farley TA, St. Germain JM, Chamberlain LA, Krassner L. The impact of influenza vaccination on respiratory illness at a boarding School. *Journal of American College Health* 1992;41(3):127-31.
64. Sonoguchi T, Naito H, Hara M. Cross-subtype protection in humans during sequential, overlapping, and/or concurrent epidemics caused by H3N2 and H1N1 influenza viruses. *Journal of Infectious Diseases* 1985;151(1):81-88.
65. Davies JR, Grilli EA, Smith AJ, Hoskins TW. Prophylactic use of amantadine in a boarding school outbreak of influenza A. *J R Coll Gen Pract* 1988;38(313):346-8.
66. Cashman P, Massey P, Durrheim D, Islam F, Merritt T, Eastwood K. Pneumonia cluster in a boarding school--implications for influenza control. *Commun Dis Intell* 2007;31(3):296-8.

67. Earn DJ, He D, Loeb MB, Fonseca K, Lee BE, Dushoff J. Effects of school closure on incidence of pandemic influenza in Alberta, Canada. *Ann Intern Med* 2012;156(3):173-81.
68. Brunyate WDT, Fleming GM, Llopis A, Roden AT. The early stages of the 1957 influenza epidemic in England and Wales in relation to the re-assembly of schools. *Mon Bull Minist Hlth Lab Serv* 1961;20(MAY):88-92.
69. Dunn FL, Carey DE, Cohen A, Martin JD. Epdemiologic studies of asian influenza in a louisiana parish. *Amer* 1959;J.Hyg. 70(3):351-71.
70. Chao DL, Halloran ME, Longini IM, Jr. School opening dates predict pandemic influenza A(H1N1) outbreaks in the United States. *J Infect Dis* 2010;202(6):877-80.
71. Jackson C, Mangtani P, Vynnycky E, Fielding K, Kitching A, Mohamed H, et al. School Closures and Student Contact Patterns. *Emerg Infect Dis* 2011;17(2):245-47.
72. Eames KTD, Tilston NL, White PJ, Adams E, Edmunds WJ. The impact of illness and the impact of school closure on social contact patterns. *Health Technol Assess* 2010;14(34):267-312.
73. Glass K, Barnes B. How much would closing schools reduce transmission during an influenza pandemic? *Epidemiology* 2007;18(5):623-8.
74. Vynnycky E, Edmunds WJ. Analyses of the 1957 (Asian) influenza pandemic in the United Kingdom and the impact of school closures. *Epidemiol Infect* 2008;136(2):166-79.
75. Milne GJ, Kelso JK, Kelly HA, Huband ST, McVernon J. A small community model for the transmission of infectious diseases: comparison of school closure as an intervention in individual-based models of an influenza pandemic. *PLoS ONE* 2008;3(12):e4005.
76. Davis LE, Caldwell GG, Lynch RE. Hong Kong influenza: The epidemiologic features of a high school family study analyzed and compared with a similar study during the 1957Asian influenza epidemic. *American Journal of Epidemiology* 1970;92(4):520.
77. Miller E, Hoschler K, Hardelid P, Stanford E, Andrews N, Zambon M. Incidence of 2009 pandemic influenza A H1N1 infection in England: a cross-sectional serological study. *Lancet* 2010;375(9720):1100-8.
78. Lowen AC, Mubareka S, Steel J, Palese P. Influenza Virus Transmission Is Dependent on Relative Humidity and Temperature. *PLoS Pathog* 2007;3(10):e151.
79. Shaman J, Goldstein E, Lipsitch M. Absolute humidity and pandemic versus epidemic influenza. *Am J Epidemiol* 2011;173(2):127-35.
80. Shaman J, Kohn M. Absolute humidity modulates influenza survival, transmission, and seasonality. *Proc Natl Acad Sci U S A* 2009;106(9):3243-8.
81. Shaman J, Pitzer VE, Viboud C, Grenfell BT, Lipsitch M. Absolute humidity and the seasonal onset of influenza in the continental United States. *PLoS Biol* 2010;8(2):e1000316.
82. Eames KT, Tilston NL, Brooks-Pollock E, Edmunds WJ. Measured Dynamic Social Contact Patterns Explain the Spread of H1N1v Influenza. *PLoS Comput Biol* 2012;8(3):e1002425.
83. Uchida M, Tsukahara T, Kaneko M, Washizuka S, Kawa S. Swine-origin influenza a outbreak 2009 at Shinshu University, Japan. *BMC Public Health* 2011;11:79.

**Table 1:** Features of the studies identified. Studies may present more than one dataset and so appear in more than one row of each section.

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| | | Number of studies |
|---|---|---|
| | ***Total studies*** | ***~~78~~79*** |
| Type of outbreak | Seasonal | 22 |
| | 1918 pandemic | ~~6~~7 |
| | 1968 pandemic | 1 |
| | 2009 pandemic | 49 |
| Setting | Europe | 22 |
| | North America | ~~21~~22 |
| | Central America | 5 |
| | South America | 3 |
| | Asia | 20 |
| | Africa | 1 |
| | Australasia | 6 |
| Data provided on[1]: | Children only | 25 |
| | General population | ~~28~~29 |
| | School pupils and staff | 5 |
| | Children and other specified groups separately | 22 |
| Reason for closure | High student absenteeism | 3 |
| | High staff absenteeism | 1 |
| | High student and staff absenteeism | 1 |
| | Other reactive closure[2] | ~~30~~31 |
| | Pro-active | 7 |
| | Planned holiday | 38 |
| | Other[3] | 3 |
| | Unclear | 3 |
| Period of closure | Continuous | 67 |
| | Intermittent | 8 |
| | Variable[4] | 3 |
| | Not stated | 1 |
| Other interventions in place[5] | None | 20 |
| | Antivirals | 33 |
| | Other social distancing | ~~23~~24 |
| | Vaccination | 8 |
| | Other | 20 |
| Timing of closure | Before peak | 21 |
| | Same day / week as peak | 9 |
| | After peak | 36 |
| | Variable[4] | 8 |
| | Unclear | ~~7~~8 |
| Duration of closure[6] | <7 days | 8 |
| | 7-13 days | 33 |
| | 14-20 days | 19 |
| | ≥21 days | 17 |
| | Variable[4] | 6 |
| | Not stated | ~~1~~2 |

[1] Each study may present more than one data source

[2] Closure in response to outbreak, not stated as being for operational reasons

[3] Teachers' strike (2 studies) or response to SARS outbreak (1 study)

[4] Studies of multiple US cities during the 1918 pandemic or multiple countries in 2009

[5] Described in the included paper or related papers; excludes normal levels of vaccine and antiviral usage in seasonal datasets.

[6] Each study may present more than one dataset for which the durations of closure differed

*Figure legends*

**Figure 1:** Identification of epidemiological studies of the effects of school closure on influenza outbreaks

**Figure 2:** Peak cumulative attack rates recorded in the identified studies. Case definitions varied between studies (see Appendix); only studies which included a denominator are shown. Studies which reported peak prevalence of absenteeism are denoted by an asterisk. See Appendix for full details of datasets. Abbreviations: BC, British Colombia; IL, Illinois; CT, Connecticut; NC, North Carolina; UK, United Kingdom; KI, Kelleys Island. All pandemic data are from 2009 except for Kelleys Island.

**Figure 3:** Normalised peak attack rates (estimated as peak attack rate / median attack rate) recorded in the identified studies; one study with an estimate normalised peak of 128 is excluded for clarity [83]. Case definitions varied between studies (see Appendix). Studies which reported peak prevalence of absenteeism are denoted by an asterisk. Abbreviations: HK, Hong Kong; IL, Illinois; SARI, severe acute respiratory infection; NC, North Carolina; UK, United Kingdom; KI, Kelleys Island.

**Box 1: Information extracted from eligible studies (where presented)**

Study design

Study population / setting (including size of population)

Nature of school closure (e.g. school holiday, response to outbreak)

Duration of closure and number of schools affected

Timing of closure in relation to influenza circulation

Outcome measure(s) examined (e.g. clinical ILI, virologically confirmed influenza)

Association between school closure and outcome

Epidemic curve (transcribed from graphs or figures); used to derive peak, cumulative and median attack rates

Normalised peak attack rate (= peak attack rate / median attack rate)

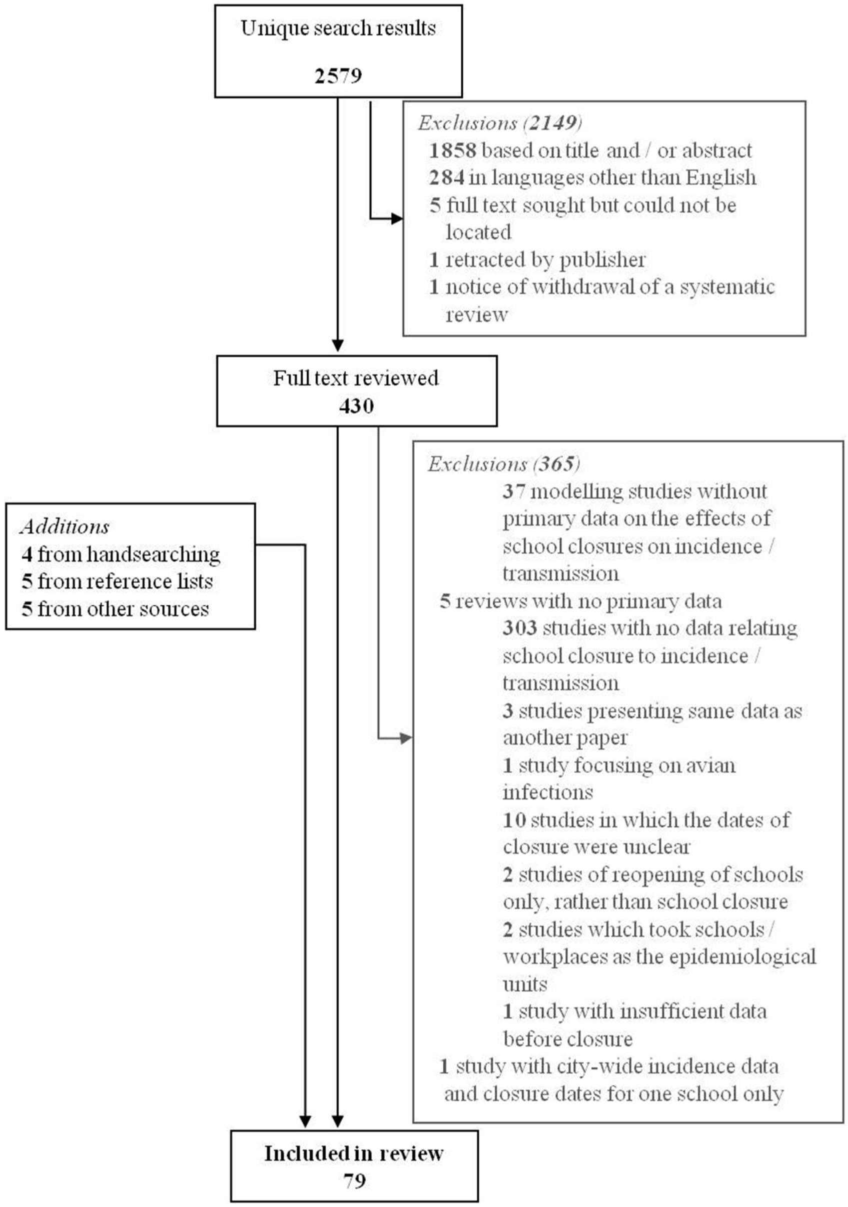



Figure 1: Identification of epidemiological studies of the effects of school closure on influenza outbreaks.
143x204mm (150 x 150 DPI)

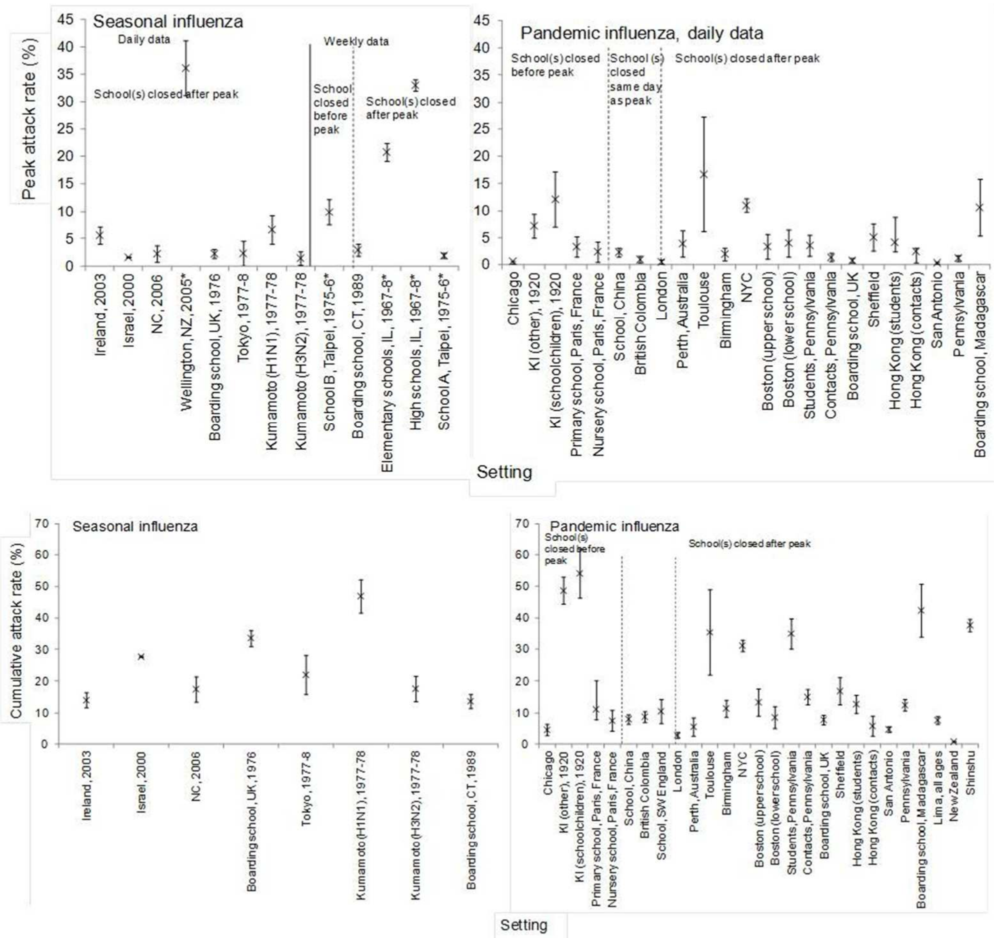



Figure 2: Peak cumulative attack rates recorded in the identified studies. Case definitions varied between studies (see Appendix); only studies which included a denominator are shown. Studies which reported peak prevalence of absenteeism are denoted by an asterisk. See Appendix for full details of datasets. Abbreviations: BC, British Colombia; IL, Illinois; CT, Connecticut; NC, North Carolina; UK, United Kingdom; KI, Kelleys Island. All pandemic data are from 2009 except for Kelleys Island.
161x152mm (150 x 150 DPI)

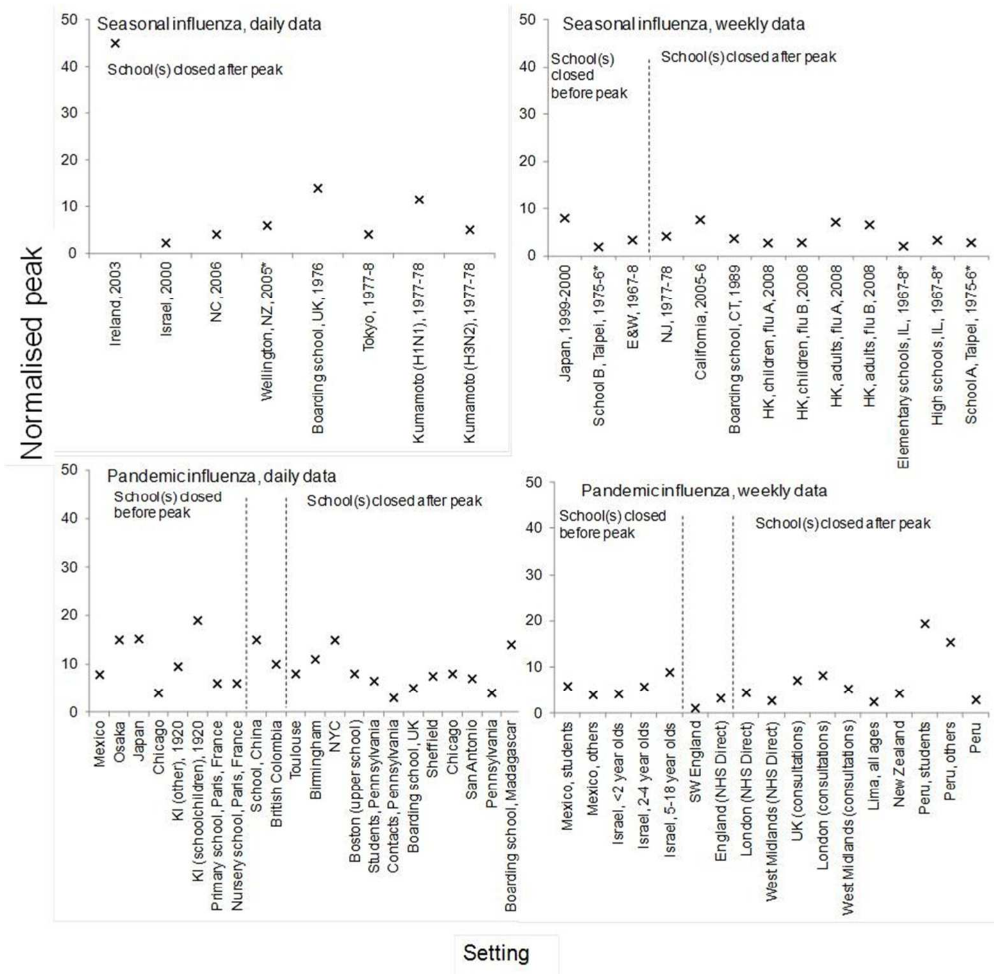



Figure 3: Normalised peak attack rates (estimated as peak attack rate / median attack rate) recorded in the identified studies; one study with an estimate normalised peak of 128 is excluded for clarity 83. Case definitions varied between studies (see Appendix). Studies which reported peak prevalence of absenteeism are denoted by an asterisk. Abbreviations: HK, Hong Kong; IL, Illinois; SARI, severe acute respiratory infection; NC, North Carolina; UK, United Kingdom; KI, Kelleys Island.
159x156mm (150 x 150 DPI)

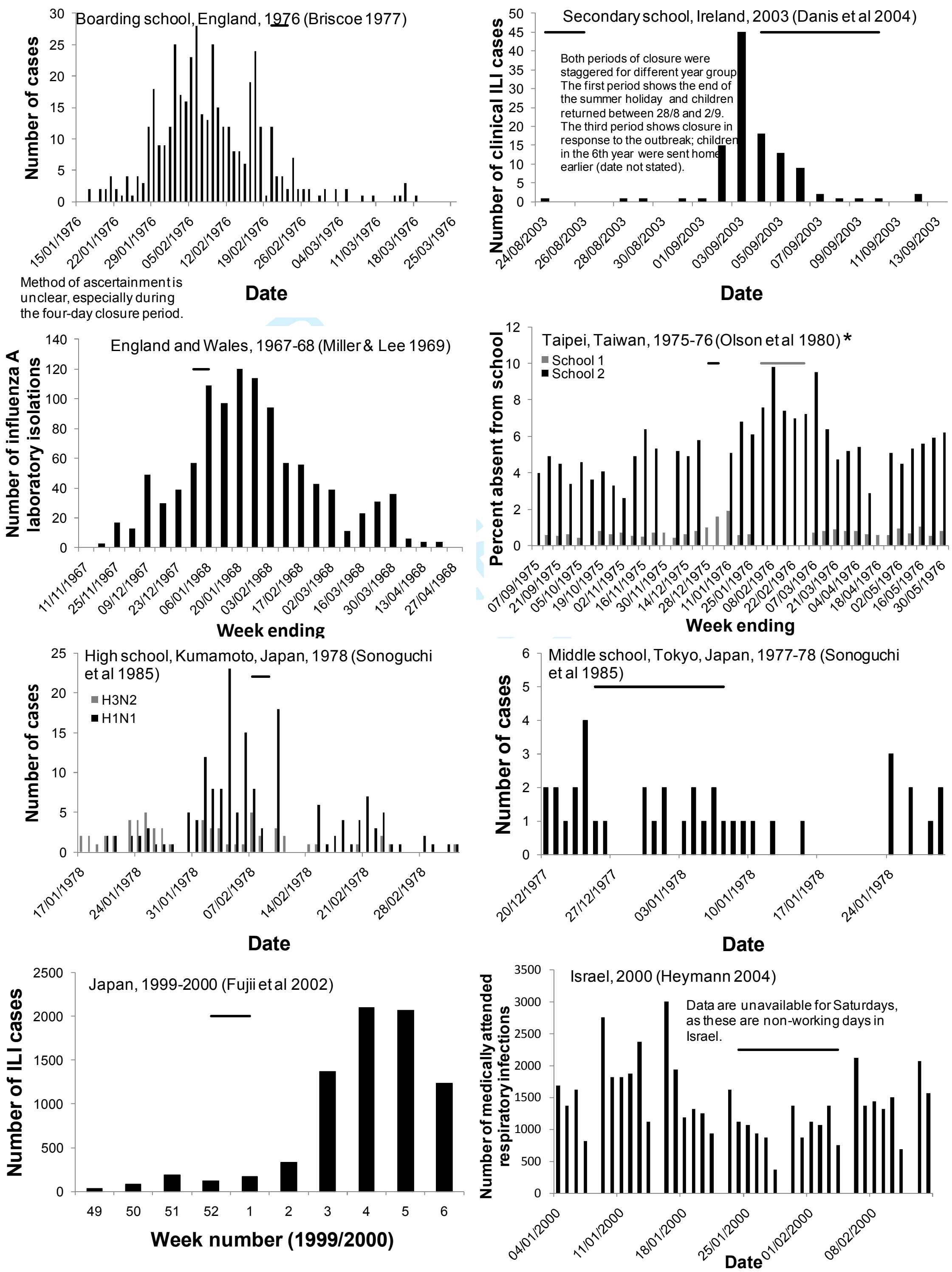
## Epidemiological evidence of the effects of school closures on influenza outbreaks: systematic review

### Supplementary Information

### Search strategy used in Medline

1. influenza.mp. or exp Influenza, Human/
2. exp Incidence/
3. exp Morbidity/
4. exp Sentinel Surveillance/ or exp Population Surveillance/
5. exp Disease Transmission, Horizontal/ or exp Acute Disease/ or exp Disease Notification/ or exp Disease Outbreaks/ or exp Communicable Disease Control/ or exp Disease/ or exp Disease Transmission/
6. (incidence or rate or morbidity or mortality or surveillance or risk or illness or death or case* or disease or infect*).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
7. (infect* or communicable or contagio*).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
8. exp Infection/
9. exp Communicable Diseases/ or exp Communicable Disease Control/ or exp Communicable Diseases, Emerging/
10. 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. ((school adj5 clos*) or (nurser* adj5 clos*) or (daycare adj5 clos*) or (day adj care adj5 clos*)).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
12. exp Schools/
13. 11 or 12
14. 1 and 10 and 13

Supplementary Figure 1: Epidemic curves for seasonal influenza. Horizontal lines show periods of school closure (weekends are shown only if they are continuous with periods of pro-active or reactive closure). Data are daily unless the x axis indicates otherwise. See Supplementary Table 1 for case definitions and full details of the datasets. School absenteeism data are denoted by an asterisk.

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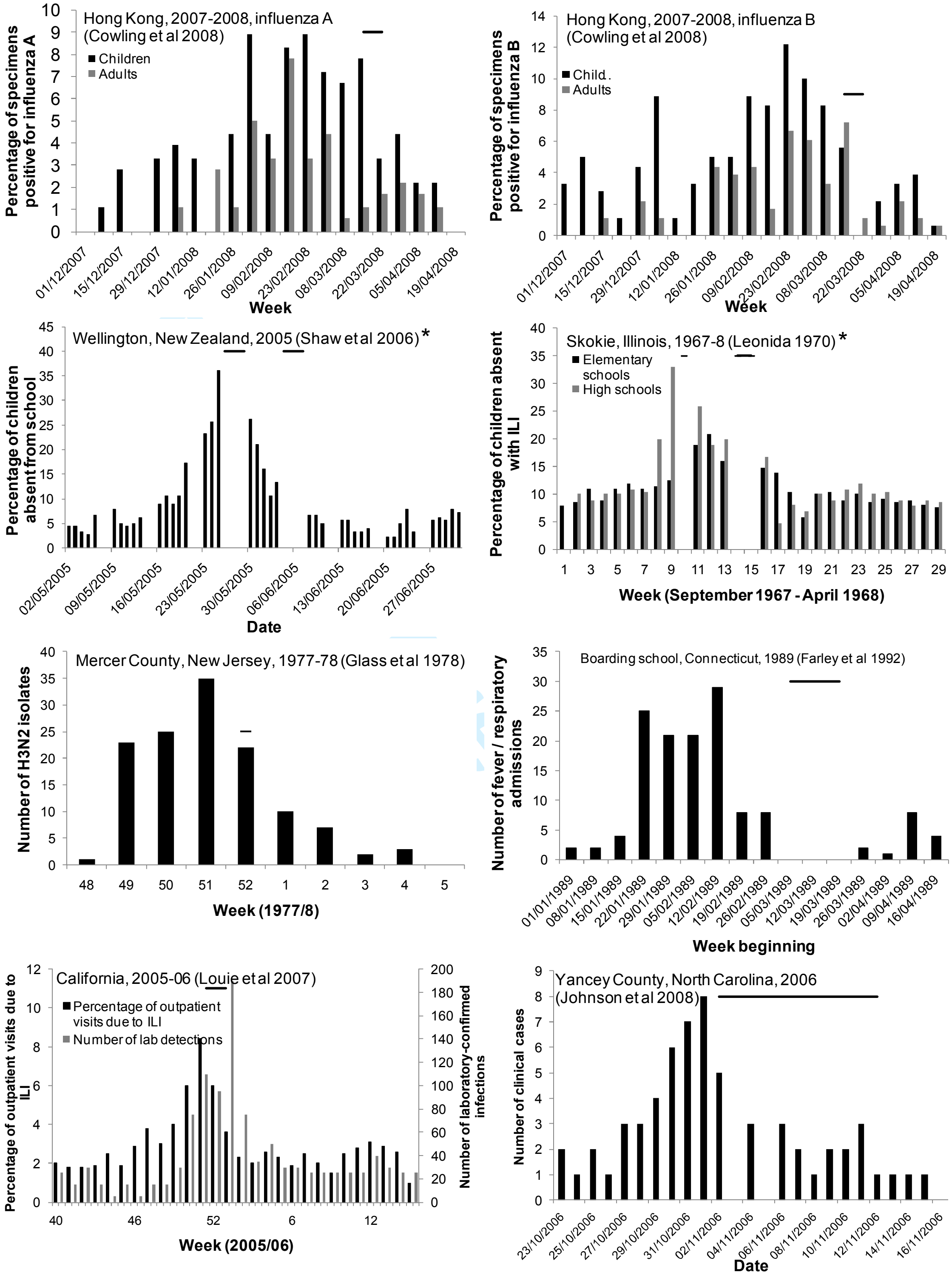
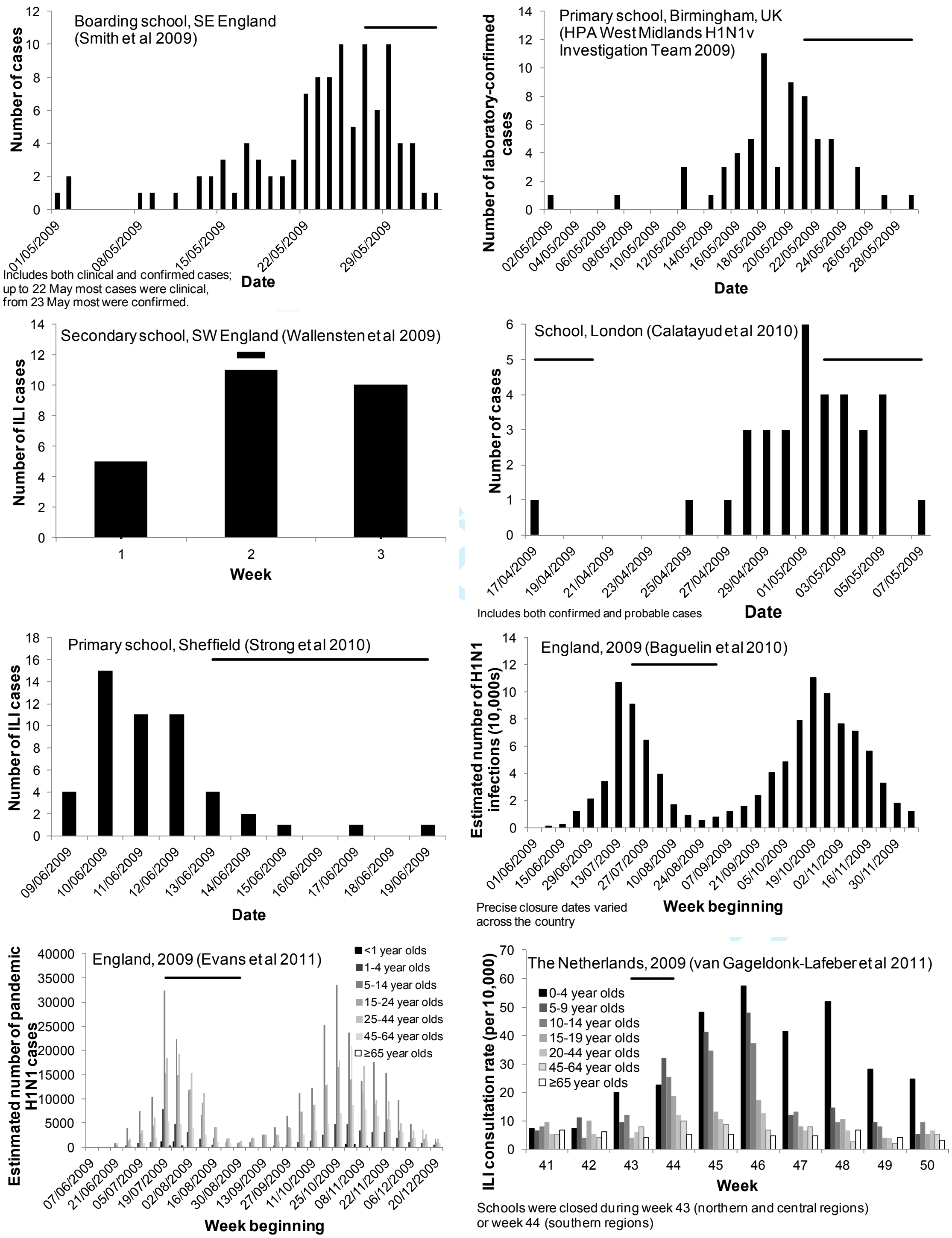
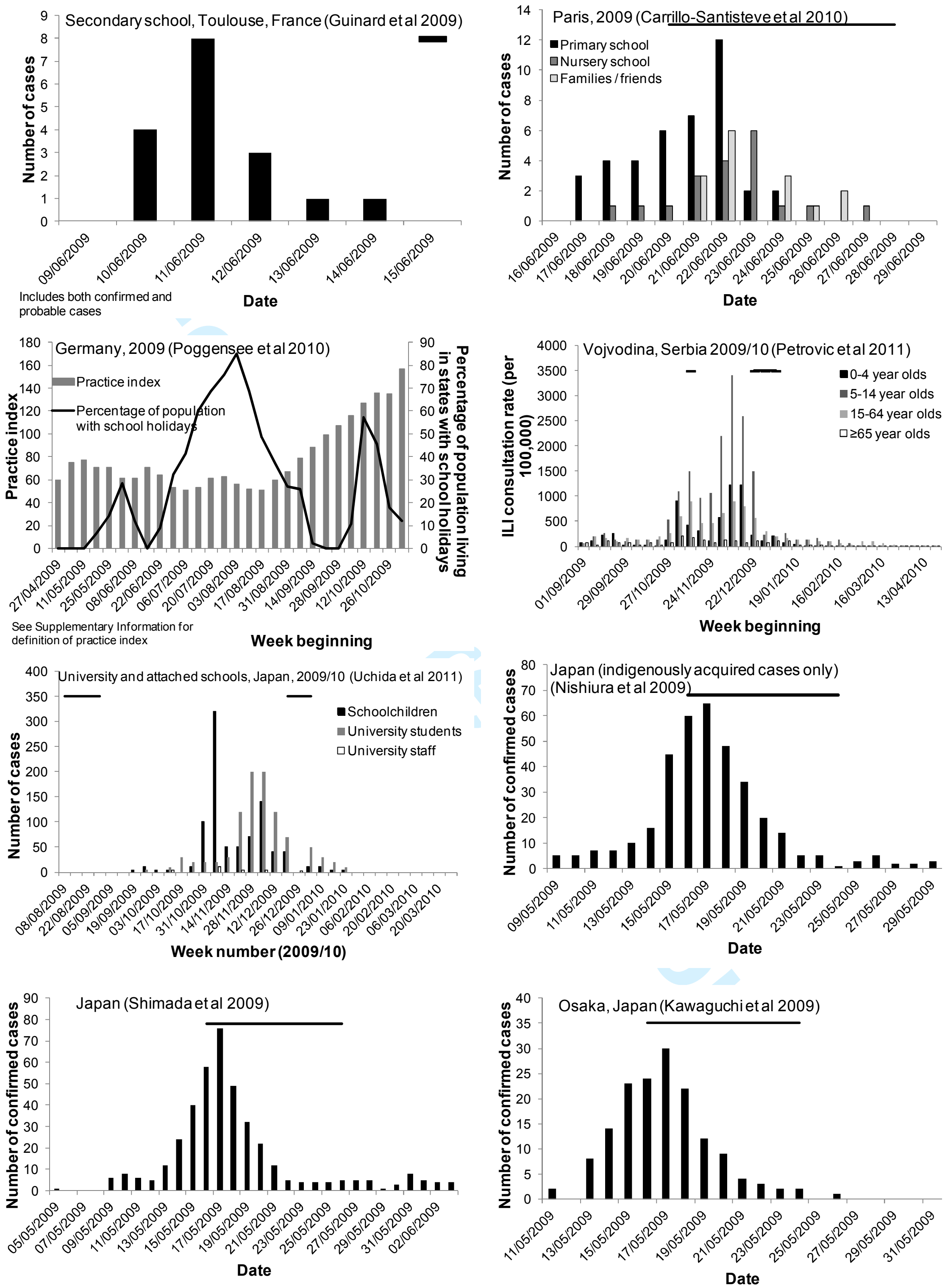

Hong Kong, 2007-2008, influenza A
(Cowling et al 2008)
Children
Adults
Percentage of specimens positive for influenza A
01/12/2007
15/12/2007
29/12/2007
12/01/2008
26/01/2008
09/02/2008
23/02/2008
08/03/2008
22/03/2008
05/04/2008
19/04/2008
Week
Hong Kong, 2007-2008, influenza B
(Cowling et al 2008)
Child.
Adults
Percentage of specimens positive for influenza B
Week
Wellington, New Zealand, 2005 (Shaw et al 2006) *
Percentage of children absent from school
02/05/2005
09/05/2005
16/05/2005
23/05/2005
30/05/2005
06/06/2005
13/06/2005
20/06/2005
27/06/2005
Date
Skokie, Illinois, 1967-8 (Leonida 1970) *
Elementary schools
High schools
Percentage of children absent with ILI
Week (September 1967 - April 1968)
Mercer County, New Jersey, 1977-78 (Glass et al 1978)
Number of H3N2 isolates
Week (1977/8)
Boarding school, Connecticut, 1989 (Farley et al 1992)
Number of fever / respiratory admissions
01/01/1989
08/01/1989
15/01/1989
22/01/1989
29/01/1989
05/02/1989
12/02/1989
19/02/1989
26/02/1989
05/03/1989
12/03/1989
19/03/1989
26/03/1989
02/04/1989
09/04/1989
16/04/1989
Week beginning
California, 2005-06 (Louie et al 2007)
Percentage of outpatient visits due to ILI
Number of lab detections
Percentage of outpatient visits due to ILI
Number of laboratory-confirmed infections
Week (2005/06)
Yancey County, North Carolina, 2006
(Johnson et al 2008)
Number of clinical cases
23/10/2006
25/10/2006
27/10/2006
29/10/2006
31/10/2006
02/11/2006
04/11/2006
06/11/2006
08/11/2006
10/11/2006
12/11/2006
14/11/2006
16/11/2006
Date

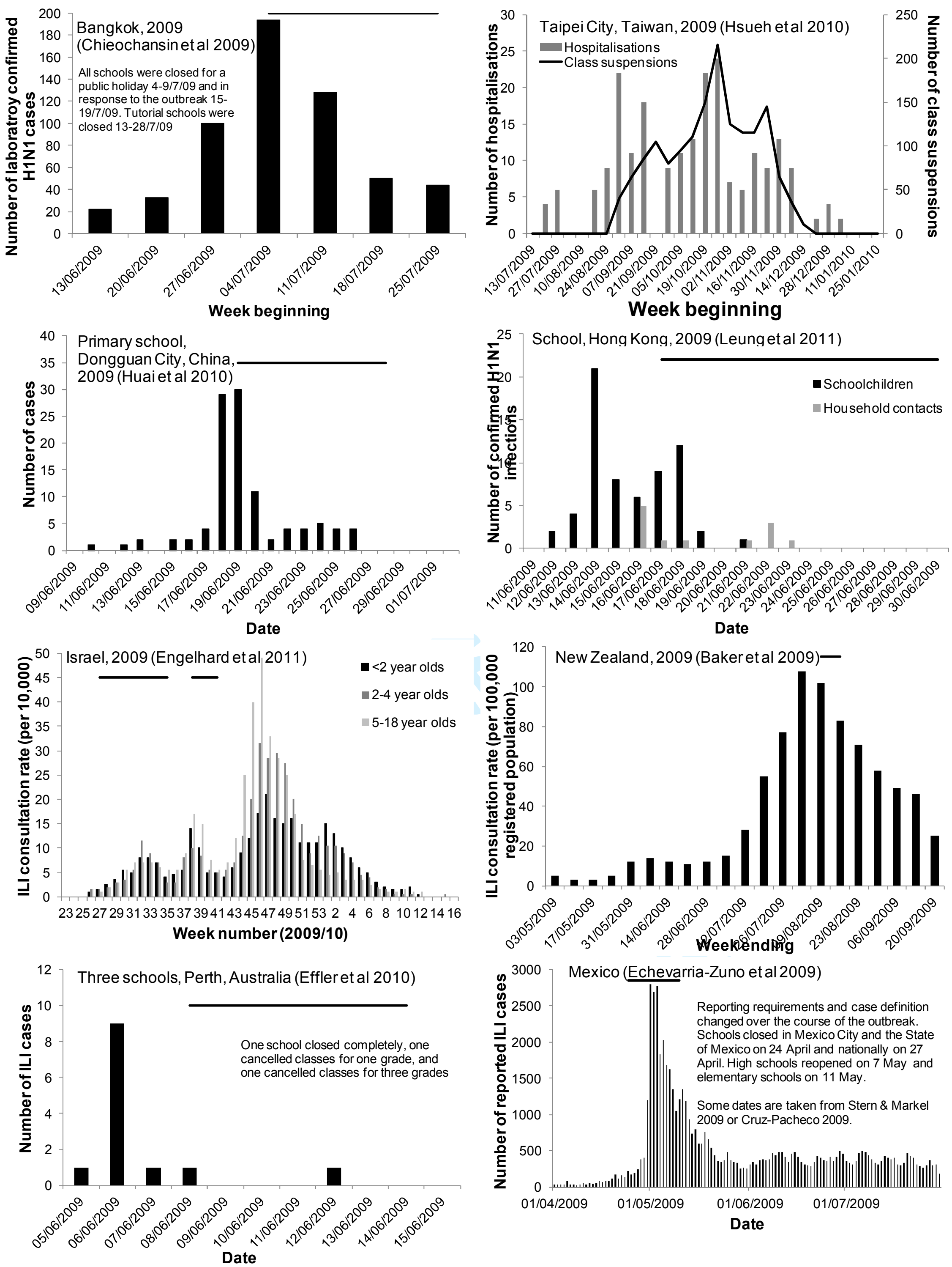
3

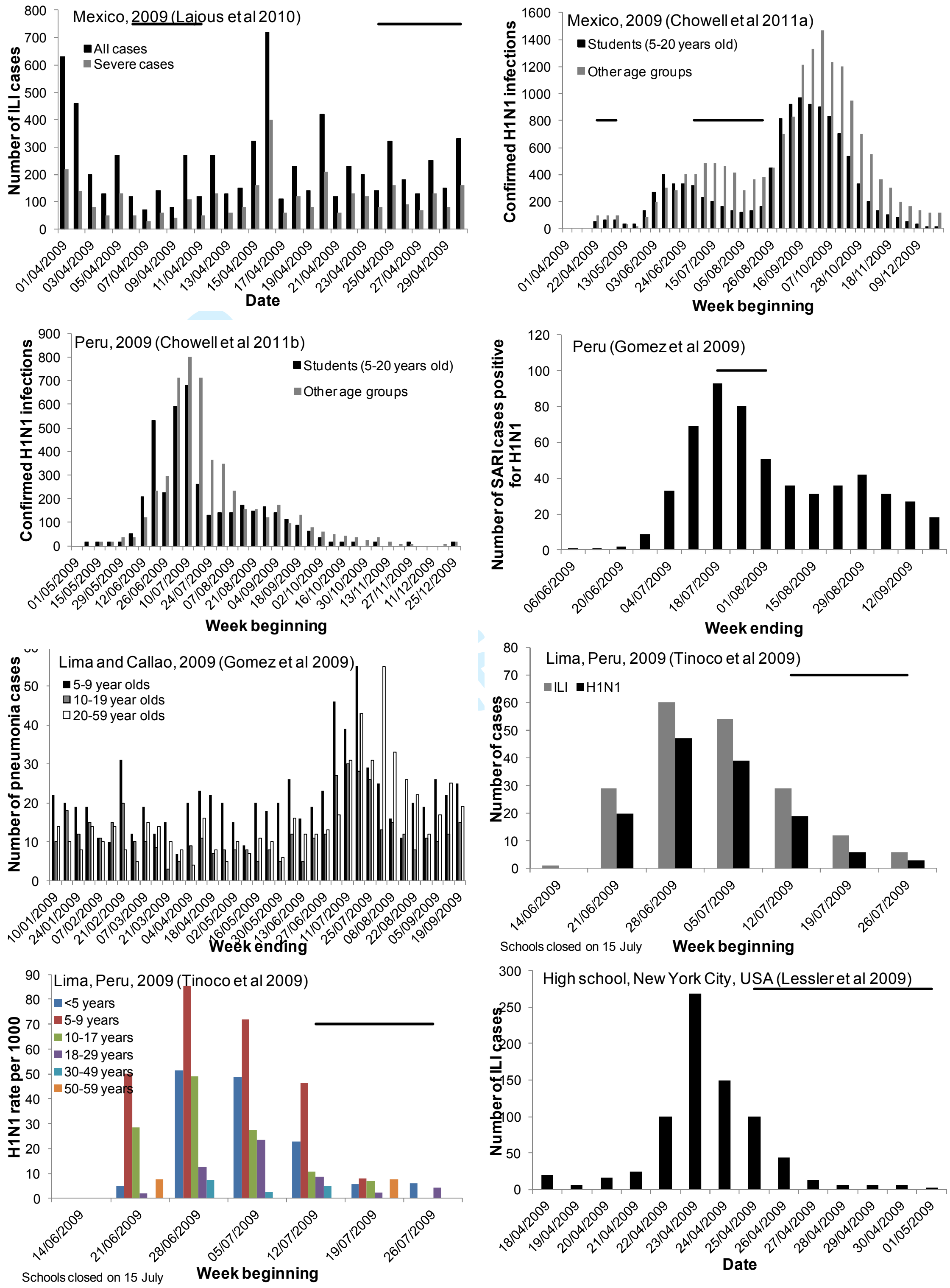
Supplementary Figure 2: Epidemic curves for pandemic influenza. Horizontal lines show periods of school closure (weekends are shown only if they are continuous with periods of pro-active or reactive closure). See Supplementary Table 2 for case definitions and full details of the datasets. School absenteeism data are denoted by an asterisk.



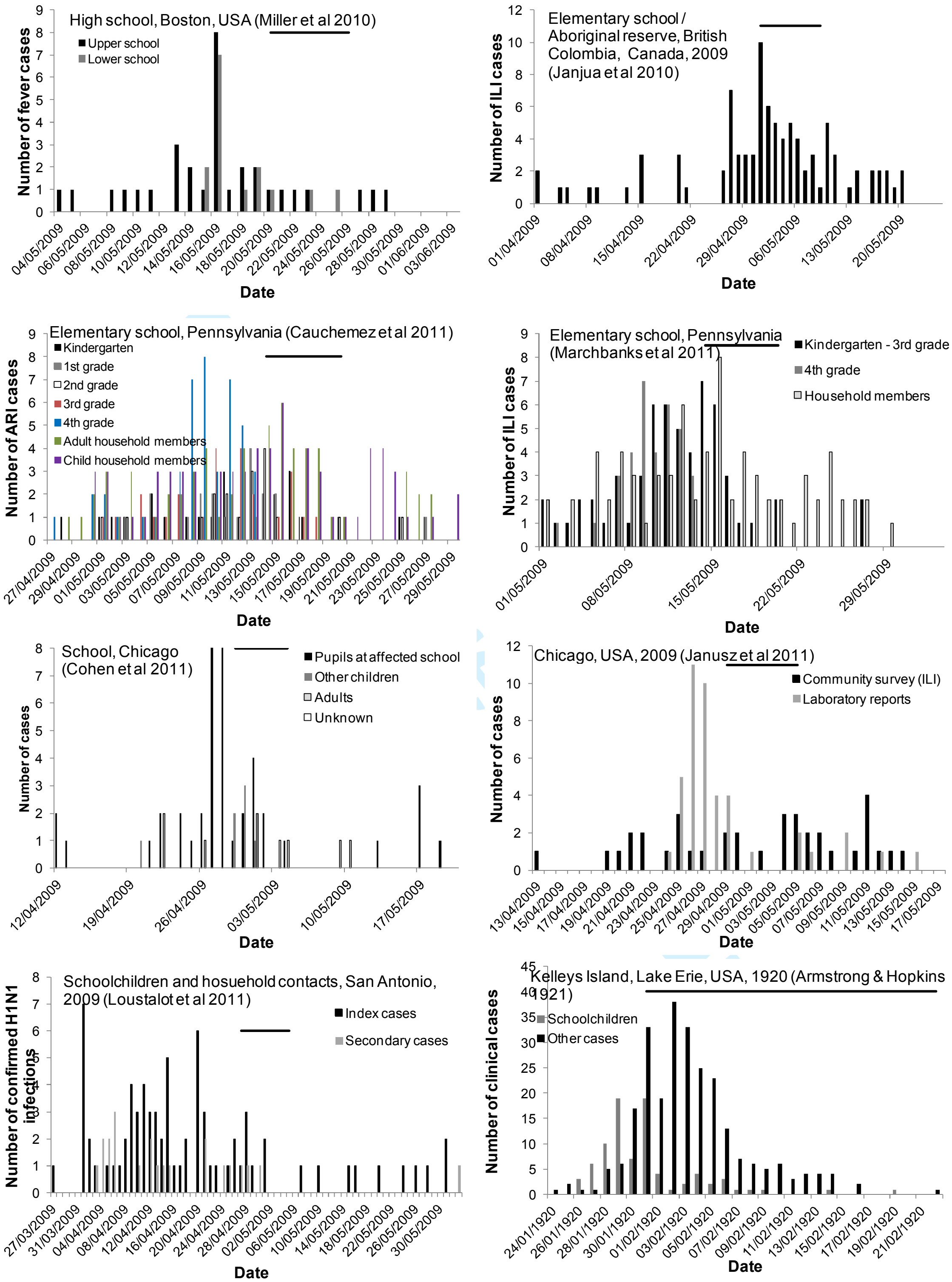

4

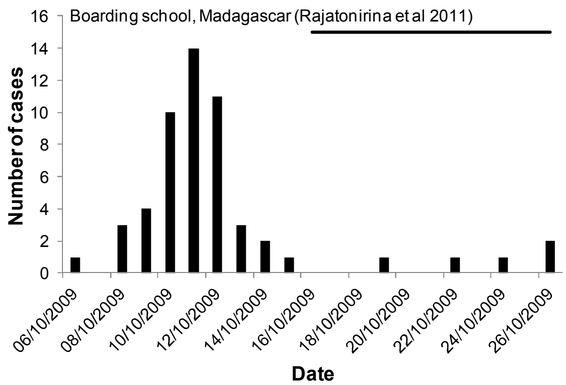

Secondary school, Toulouse, France (Guinard et al 2009)
Number of cases
Date
Includes both confirmed and probable cases
Paris, 2009 (Carrillo-Santisteve et al 2010)
Primary school
Nursery school
Families / friends
Number of cases
Date
Germany, 2009 (Poggensee et al 2010)
Practice index
Percentage of population with school holidays
Practice index
Percentage of population living in states with school holidays
Week beginning
See Supplementary Information for definition of practice index
Vojvodina, Serbia 2009/10 (Petrovic et al 2011)
0-4 year olds
5-14 year olds
15-64 year olds
≥65 year olds
ILI consultation rate (per 100,000)
Week beginning
University and attached schools, Japan, 2009/10 (Uchida et al 2011)
Schoolchildren
University students
University staff
Number of cases
Week number (2009/10)
Japan (indigenously acquired cases only) (Nishiura et al 2009)
Number of confirmed cases
Date
Japan (Shimada et al 2009)
Number of confirmed cases
Date
Osaka, Japan (Kawaguchi et al 2009)
Number of confirmed cases
Date


Bangkok, 2009 (Chieochansin et al 2009)
All schools were closed for a public holiday 4-9/7/09 and in response to the outbreak 15-19/7/09. Tutorial schools were closed 13-28/7/09
Number of laboratroy confirmed H1N1 cases
Week beginning
Taipei City, Taiwan, 2009 (Hsueh et al 2010)
Hospitalisations
Class suspensions
Number of hospitalisations
Number of class suspensions
Week beginning
Primary school, Dongguan City, China, 2009 (Huai et al 2010)
Number of cases
Date
School, Hong Kong, 2009 (Leung et al 2011)
Schoolchildren
Household contacts
Number of confirmed H1N1 infections
Date
Israel, 2009 (Engelhard et al 2011)
<2 year olds
2-4 year olds
5-18 year olds
ILI consultation rate (per 10,000)
Week number (2009/10)
New Zealand, 2009 (Baker et al 2009)
ILI consultation rate (per 100,000 registered population)
Week ending
Three schools, Perth, Australia (Effler et al 2010)
One school closed completely, one cancelled classes for one grade, and one cancelled classes for three grades
Number of ILI cases
Date
Mexico (Echevarria-Zuno et al 2009)
Reporting requirements and case definition changed over the course of the outbreak. Schools closed in Mexico City and the State of Mexico on 24 April and nationally on 27 April. High schools reopened on 7 May and elementary schools on 11 May.
Some dates are taken from Stern & Markel 2009 or Cruz-Pacheco 2009.
Number of reported ILI cases
Date



Mexico, 2009 (Lajous et al 2010)
All cases
Severe cases
Number of ILI cases
Date
Mexico, 2009 (Chowell et al 2011a)
Students (5-20 years old)
Other age groups
Confirmed H1N1 infections
Week beginning
Peru, 2009 (Chowell et al 2011b)
Students (5-20 years old)
Other age groups
Confirmed H1N1 infections
Week beginning
Peru (Gomez et al 2009)
Number of SARI cases positive for H1N1
Week ending
Lima and Callao, 2009 (Gomez et al 2009)
5-9 year olds
10-19 year olds
20-59 year olds
Number of pneumonia cases
Week ending
Lima, Peru, 2009 (Tinoco et al 2009)
ILI
H1N1
Number of cases
Schools closed on 15 July
Week beginning
Lima, Peru, 2009 (Tinoco et al 2009)
<5 years
5-9 years
10-17 years
18-29 years
30-49 years
50-59 years
H1N1 rate per 1000
Schools closed on 15 July
Week beginning
High school, New York City, USA (Lessler et al 2009)
Number of ILI cases
Date


High school, Boston, USA (Miller et al 2010)
Upper school
Lower school
Number of fever cases
Date
Elementary school / Aboriginal reserve, British Colombia, Canada, 2009 (Janjua et al 2010)
Number of ILI cases
Date
Elementary school, Pennsylvania (Cauchemez et al 2011)
Kindergarten
1st grade
2nd grade
3rd grade
4th grade
Adult household members
Child household members
Number of ARI cases
Date
Elementary school, Pennsylvania (Marchbanks et al 2011)
Kindergarten - 3rd grade
4th grade
Household members
Number of ILI cases
Date
School, Chicago (Cohen et al 2011)
Pupils at affected school
Other children
Adults
Unknown
Number of cases
Date
Chicago, USA, 2009 (Janusz et al 2011)
Community survey (ILI)
Laboratory reports
Number of cases
Date
Schoolchildren and hosuehold contacts, San Antonio, 2009 (Loustalot et al 2011)
Index cases
Secondary cases
Number of confirmed H1N1 infections
Date
Kelleys Island, Lake Erie, USA, 1920 (Armstrong & Hopkins 1921)
Schoolchildren
Other cases
Number of clinical cases
Date


Boarding school, Madagascar (Rajatonirina et al 2011)
Number of cases
16
14
12
10
8
6
4
2
0
06/10/2009
08/10/2009
10/10/2009
12/10/2009
14/10/2009
16/10/2009
18/10/2009
20/10/2009
22/10/2009
24/10/2009
26/10/2009
Date

**Supplementary Table 1: Studies of the effects of school closures on seasonal influenza outbreaks**

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| **Europe** | | | | | | | |
| Briscoe (1977) [1] | Outbreak report / estimate of vaccine efficacy | 1231 boys at Eton College, 1976 (79% of whom were vaccinated). Age of pupils not stated but the school currently takes boys aged 13-18. | Planned half term holiday | Friday 20 to Monday 23 February | Epidemic began in late January, first wave peaked 6 February, second wave peaked 17 February. | Clinical influenza (n = 372); confirmed as influenza A in 6/8 swabbed cases and influenza B in 1/8. | One case on day before break, ~12 cases on following day. ~1-4 cases/day for rest of study period. Hypothesised that closure curtailed the epidemics in individual school houses. 15/26 houses had no further cases after the break. |
| Davies et al (1988) [2] | Non-controlled intervention study of prophylactic amantadine | 859 boys aged 11-18 years at Christ's Hospital boarding school, 1986 | Planned half term holiday | Friday 21 to Monday 24 February | Epidemic began in early February, prophylaxis began on 5 February coinciding with the peak | Clinical influenza (n = 181); confirmed as influenza A H3N2 in majority of cases | 0-3 cases/day in five days preceding closure; 12 cases over 4-day closure period. Daily case numbers immediately following re-opening similar to those before closure. |
| Grilli et al (1989) [3] | Outbreak report | 675 boys aged 11-18 years at Christ's Hospital boarding school, 1985 | Planned mid-term break | 22-24 February | Epidemic began in late January and appeared to peak (at ~19 cases) 4 days before closure | ILI in pupils reporting to school infirmary (n = 206), the majority of which were confirmed as influenza. | 4-5 cases on each of the 2 days before closure; 15 cases occurred during closure (no daily breakdown is provided). ~0-6 cases occurred per day over the month following reopening. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Danis et al (2004) [4] | Outbreak report | 802 pupils at boys' secondary school (age 11-18 years), Ireland, 2003 | Response to outbreak | Whole school closed 4-11 September; 6th class sent home earlier (date not stated) | Whole school closure from day after peak of outbreak | ILI in absentees ascertained through telephone and questionnaire surveys (n = 107); confirmed as influenza in 12/15 cases | Peak incidence ~45 cases on day before closure; 18 cases on first day of closure and continuing decline thereafter. Only 2 cases after re-opening (although there was no active case finding at this point). Little evidence of community spread after the school outbreak. |
| Miller and Lee (1969) [5] | Outbreak report | England and Scotland (all ages), November 1967 – February 1968 | Planned Christmas holiday | Two weeks, all schools | Schools closed during the growth phase of the epidemic in most age groups | Age-specific rates of influenza reported by general practitioners | Rates in 0-4, 15-44, 45-64 and ≥65 year olds peaked during the second week of closure, rates in 5-14 year olds were in decline at this point. Following reopening, increases occurred in the 0-4 and especially 5-14 year age groups. |
| Cauchemez et al (2008) [6] | Statistical / transmission modelling analysis based on fitting to surveillance data | French national sentinel surveillance system, 1985-2006 (covering all ages, over 60 epidemic periods and from ~1% of practicing GPs) | Routine school holidays | Approx 2 weeks in each of December – January, February – March, March-April. Timing varies by 1-2 weeks in the 2-3 holiday zones. | Varied between epidemics | Rates of influenza-like illness reported through sentinel GPs | Estimated that holidays resulted in a 20-29% (median 24%) decrease in rate of transmission to children, without affecting contacts made by adults; this translated to a reduction in the attack rate of 16-18% overall (14-17% for adults, 18-21% for children) |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| **Asia** | | | | | | | |
| Olson et al (1980) [7] | Outbreak report | Grades 1-6 (2831 students) of Girls Teachers' Colleges Primary School, Taipei and grades 1-6 (650 students) of Taipei American School , Taiwan, September 1975 – May 1976. Ages of students not stated. | Planned holiday during virologically confirmed community influenza outbreak | Six weeks (Girls Teachers' Colleges Primary School); 3 weeks (Taipei American School) | Relationship with influenza circulation unclear, but likely to be late in the outbreak. Absenteeism at Girls Teachers' Colleges Primary School peaked two weeks before closure; absenteeism at Taipei American School had not exceeded the epidemic threshold at the time of closure. | School absenteeism (all cause) | Girls Teachers' Colleges Primary School: absenteeism declined from ~1.65 absences per child-day in the week before closure to ~0.7 absences per child-day (only slightly above expected absenteeism of 0.65) in the week following re-opening. Taipei American School: absenteeism very similar before and after closure |
| Sonoguchi et al (1985) [8] | Cohort study of the extent of cross-protection between influenza subtypes | 173 children (of 245 enrolled) aged 13-14 at a middle school in Tokyo; 347 children (of 374 enrolled) at a high school in Kumamoto prefecture, Japan. >90% vaccination coverage at each school. | Planned winter holiday (middle school); response to high levels of absenteeism (high school) | Two weeks (middle school); 3 days (high school) | Middle school: case numbers were fairly constant at <5/day during the week before closure. High school: epidemic appeared to be in decline when school closed but case numbers increased on reopening. | Absenteeism while the schools were open; serious, confirmed influenza A infection during closure periods. | Middle school: case numbers remained low at 0-2 per day during closure. High school: case numbers declined from 16 on the day before closure to 13, 5 and 0 on the three days of closure, rebounding to 21 on the day of reopening. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Fujii et al (2002)[9] | Presentation of surveillance data | Children aged 4-14 years attending 36 sentinel surveillance in Japan, 1999-2000 | Planned holiday | 2 weeks | Case numbers began to increase from week 50 of 1999; schools closed week 52 and week 1. | Medically attended clinical ILI | 191 cases in week before closure, declining by 38% to 118 cases during the first week of closure. Incidence increased to 173 cases during the second week of closure and an epidemic followed when schools reopened. |
| Heymann et al (2004)[10] | Ecological before-and-after comparison | All 6-12 year old children (n = 186094) registered with one of the four national healthcare insurance schemes, Israel, 2000 | National teachers' strike affecting ~80% of 6-12 year old children[11] coinciding with influenza outbreak | 2 weeks (16-28 January 2000), elementary schools nationwide. Ultra-orthodox schools, preschools and high schools remained open. | Outbreak began in last week of December 1999; schools closed 16-28 January 2000. | Medically attended / diagnosed respiratory tract infections (MARI); All physician visits; All outpatient clinic visits; All emergency department visits; hospitalisations; medication purchases (antibiotics, antipyretics, cold and cough medicines). | MARI: number of cases decreased by 42% and 27% during closure period and following fortnight respectively, compared to the fortnight before the closure.* Physician visits: rate ratios 0.78 and 0.88* No effect on hospital admissions. |
| Lo et al (2005)[12] | Ecological before-and-after comparison | Respiratory specimens (all ages) processed by Government Virus Unit, Hong Kong, 1998-2003 | Reaction to SARS outbreaks; other social distancing and hygiene measure also implemented | Not stated, but general community control measures were in effect at least in April – June 2003 | Not clear | Proportion of respiratory specimens positive for influenza | Monthly proportions positive were 58-88% lower in April – June 2003 than the average for the corresponding months of 1998-2003, but the difference with specific years was variable (e.g. little difference with the low influenza years of 1999 and 2000). |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Cowling et al (2008) [13] | Ecological before-and-after comparison with modelling analysis | Hong Kong population (all ages), 2008 | Reactive closure for 1 week in response to 3 influenza deaths in children, followed by scheduled 1 week Easter break. | 2 weeks (including Easter break) – all primary schools, special schools, kindergartens and day nurseries. | Outbreak began in January and peaked in February; schools closed 13 March. | Influenza A and B isolations from surveillance data as proportion of all specimens (for children and adults separately); sentinel ILI consultation rates; influenza hospital admission rates in children aged <5 years; estimates of effective reproduction number. | Continued decrease in already declining incidence measures; no apparent meaningful change in effective reproduction number. |
| Heymann et al (2009) [11] | Ecological before-and-after comparison, with comparison to years not affected by atypical school closure | Individuals aged ≥6 years registered with a specific healthcare service provider in Israel, 1998-2002 | Teachers' strike affecting ~80% of children, coinciding with influenza outbreak in 2000; Hanukah holidays in all years. | 8 days each year for Hanukah holiday; 2 week closure (16-28 January 2000) of elementary schools nationwide, excluding ultra-orthodox, preschools and high schools. | Closure due to strike as Heymann (2004) [10]; timing of Hanukah holidays in relation to respective epidemics not clear. | Ratio of number of clinic visits for ILI to number for non-respiratory illness, in 6-12 year olds and individuals aged over 12 (calculated separately for those living with and without 6-12 year olds). | Decrease in ratio of 15% for 6-12 year olds associated with the strike; decreases in adults were not statistically significant. In some years, there was evidence of a reduction in the ratio for adults and/or children associated with the Hanukah holidays. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| **Australasia** | | | | | | | |
| Cashman et al (2007) [14] | Outbreak report | Secondary boarding / day school (age of pupils not stated), New South Wales, Australia, August 2006 | Planned closure coinciding with outbreak of ILI and pneumonia | Four days | Unclear, but closure appears to have occurred late in outbreak | Presentations to sick bay with respiratory illness (n not stated). Influenza A H3N2 isolated from 5 students | Respiratory presentations decreased following closure, returning to baseline within 7 days (no further quantitative information provided). |
| Shaw et al (2006) [15] | Outbreak report | Single school in Wellington, New Zealand, May-June 2005 – 350 pupils in years 1-8. | One closure in response to high levels of absenteeism; later closure for a “holiday weekend” | Two closures of 4 days each, including weekends in both cases | Peak absenteeism occurred on the day before the first closure; epidemic was generally declining before the second closure | School absenteeism (all causes) | For both closures, absenteeism was lower on reopening than before the closure. |
| **Americas** | | | | | | | |
| Leonida (1970) [16] | Outbreak report | Five elementary schools (student population 2314) and three high schools (student population 8012) in Skokie, Illinois, September 1967 – April 1968 | Winter holiday | One week at the end of November and two weeks at the end of December; all schools in the sample | First closure 2 weeks before peak in elementary schools and 2 weeks after peak in high schools; second closure 2 weeks after peak in elementary schools and 6 weeks after peak in high schools. | School absenteeism due to ILI. | First closure had no clear effect on the increase in absenteeism at the elementary schools or the decline in the high schools. Absenteeism continued to decline in both elementary and high schools during the second closure; no apparent increase on reopening. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Glass et al (1978) [17] | Outbreak report | Mercer County, New Jersey, USA, November 1977 – March 1978 | Planned Christmas holiday | One week (public schools) or two weeks (residential schools) | Around peak of outbreak | Absenteeism from 6 public schools, work absenteeism, febrile illnesses in nursing homes, admissions to three residential school infirmaries, emergency room visits, hospital admissions for acute respiratory disease, P&I deaths, viral isolates | School absenteeism was lower after the holiday than before and gradually increased, reaching a plateau at a level slightly higher than before the closure. Emergency room visits and hospital admissions peaked during the closure week and viral isolates the week before. |
| Farley et al (1992) [18] | Outbreak report / estimate of vaccine efficacy | Boarding school, Connecticut (989 pupils in grades 9-12), January – April 1989 | Planned holiday | Three weeks | Epidemic appeared to be largely over by the time of the holiday (there were ~8 cases in the week before closure; the peak had occurred 5 weeks previously) | Admission to school infirmary with fever or respiratory symptoms ( n ~135) | Number of admissions remained low (≤8 per week) after reopening. |
| Louie et al (2007) [19] | Description of several surveillance systems during one influenza season | California, week 40 of 2005 to week 15 of 2006 | Planned winter holiday | Two weeks; presumably all schools | ILI peaked week before closure; laboratory isolations appeared to be increasing when schools were closed. | ILI reported through sentinel surveillance system (expressed as the proportion of all visits that were for ILI); number of laboratory-confirmed influenza from sentinel laboratories. | ILI declined throughout school closure and remained at low levels following reopening; laboratory-confirmed infections declined slightly in the first week of closure, then increased before declining after schools reopened. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Johnson et al (2008) [20] | Outbreak report focussing on effects of closure on families | 355 children enrolled in all 9 public elementary, middle and high schools in Yancey County, North Carolina, USA, 2006. | Closure for operational reasons, due to high levels of staff absenteeism largely attributed to ILI. | 10 days (2 – 12 November) - all 9 schools in the county. | First reported onset (in study sample) 20 October, epidemic peak 1 November, schools closed 2 November. | Parentally-reported ILI (n = 123) ascertained through telephone survey | Incidence decreased from peak of 8 cases the day before closure to 5 cases on the first day of closure, and continued to decline thereafter. |
| Rodriguez et al (2009) [21] | Cohort study comparing schools which cancelled their winter break to those which did not | 265 elementary, middle, high and “other” schools which closed and 205 which did not, King County, Washington, February – March 2007 | Planned holiday closure coinciding with influenza outbreak | 1 week, including middle, high and other public and private schools | Closure immediately following epidemic peak | School absenteeism (all causes) | No evidence of a difference in absenteeism following the break between schools that closed and those that did not. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Wheeler et al (2010) [22] | Ecological before-and-after comparison covering fortnights before, during and after school closure in 4 influenza seasons. | General population of Arizona, 2004/05 – 2007/08 influenza seasons. | Planned winter holidays | 2 weeks, all schools in the state | Peak occurred at least 2 weeks after reopening in 3 of the 4 seasons; peak coincided with the second week of closure in the remaining season. | Influenza laboratory reports 2004/05 to 2007/08 (n = 833 in school-aged children, 4036 in other age groups); influenza hospitalisations 2004/05 to 2006/07 (n = 885 in school-aged children, 4512 in other age groups). | For school-aged children, incidence never significantly increased during the two weeks of closure compared to the preceding two weeks; incidence in the two weeks following reopening either increased (2 seasons), declined (1 season) or was unchanged compared to the weeks of closure.<br>For other age groups, incidence consistently increased during the closure period; changes on reopening were inconsistent. |

* Recalculated from data provided in paper

## Supplementary Table 2: Studies of the effects of school closures on pandemic influenza

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| **Europe** | | | | | | | |
| Smith et al (2009) [23] | Outbreak report | 1307 pupils aged 13-18 at a boarding school in SE England, May – June 2009 | Scheduled break extended in response to outbreak; prophylactic oseltamivir also used | 11 days (4 day scheduled break extended by 7 days). Some pupils returned ~1 week earlier for exams | Closed around time of epidemic peak | Clinical ILI in pupils attending school healthcare facilities 1-27 May; laboratory-confirmed H1N1v after 27 May (n = 102 including both clinical and confirmed cases) | Apparent decline in cases in pupils following closure; no information on other age groups |
| HPA West Midlands H1N1v Investigation Team (2009) [24] | Outbreak report | 479 primary and nursery school pupils (aged 4-12), plus 84 staff, at a school in Birmingham, England, May 2009 | Scheduled break extended in response to outbreak; prophylactic oseltamivir also used | 11 days (9 day scheduled break extended by 2 days) | After epidemic peak | Laboratory confirmed H1N1v (n = 64) | Case numbers in pupils and staff declined following closure (e.g. from 8 cases on the day of closure to 5 on each of the two following days). No further cases following re-opening. Limited information on illness in other groups. |
| Wallensten et al (2009) [25] | Outbreak report | 248 Year 7 pupils at a school in SW England (93% of the year group, aged 11-12 years), April – May 2009 | Response to outbreak; prophylactic oseltamivir also used | 10 days | Unclear | Prevalence of self-reported ILI during the week before closure, the closure week, and the following week | 5, 11 and 10 children had symptoms compatible with the case definition in the week before, during and after closure, respectively. Absenteeism was almost identical in the weeks before and after closure. No information on illness in other age groups. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Calatayud et al (2010) [26] | Outbreak report | 1177 pupils (year groups Reception to 13), plus staff, at a school in London, May 2009 | Response to outbreak (preceded by closure for Easter several weeks previously); use of prophylactic oseltamivir | 3 days of Easter holiday remained after onset of first possible case; reactive closure lasted 9 days (including 2 weekends). | One possible case occurred 3 days before the end of the Easter closure and did not attend school while symptomatic; no further cases occurred until the main outbreak began ~7-10 days after this possible case. Reactive closure occurred the day following the peak (6 cases). | Virologically confirmed or possible (symptomatic without combined nose and throat swab but pending serological results) H1N1 infection | Cases continued to occur at 3-4 cases / day for 4 days following reactive closure. On the 5th and 6th days, there were 0 and 1 cases, respectively, and no cases subsequent to this. |
| Strong et al (2010) [27] | Outbreak report, focussing on use of antivirals | 297 pupils (aged 7-12 years) and 58 staff at a primary school in Sheffield, June 2009 | Response to outbreak; oseltamivir used for treatment and prophylaxis | One week | Epidemic peaked 3 days before closure. | Self-reported ILI (n = 61) | Incidence continued to decline while school was closed; no data presented for period after reopening. |
| Baguelin et al (2010) [28] | Modelling study of cost-effectiveness of vaccination; includes incidence data spanning term time and holiday periods. | England & Wales population, June – October 2009. | Planned summer holiday. | ~ 6 weeks, all schools nationally. | Closure coincided with peak of the first wave. | Health Protection Agency estimates of numbers of infections, rescaled (multiplied by 10) to reflect under-reporting. | Incidence declined throughout the period of school closure and increased after schools reopened, producing a second wave of infection. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Guinard et al (2009) [29] | Outbreak report | 30 students (aged 11-12 years) and 18 staff from one affected class, at a secondary school in Toulouse, France, June 2009 | Reactive closure in response to outbreak; some use of prophylactic oseltamivir | 7 days | At apparent end of epidemic | Probable H1N1v infection with or without laboratory confirmation (n = 17 with known date of onset, plus 3 without) | No further cases in pupils or their contacts following closure, but epidemic appeared to be over before the school was closed. |
| Carrillo-Santisteve et al (2010) [30] | Outbreak report | Two primary schools (360 and 293 aged 6-11 years), a nursery school (253 children aged 3-6 years) and a daycare school (unknown number of children aged 3 months to 3 years), Paris, June 2009; the four schools shared some facilities. | Response to outbreak which began in one of the primary schools; close contacts were given prophylactic oseltamivir. | 9 days (including 2 weekends), one of the primary schools and the nursery school (these schools accounted for 59/66 cases in pupils) | Officially closed on day of peak, but weekend began two days previously. | Confirmed and probable influenza cases in children attending the closed schools and their families and friends who consulted influenza outpatient clinic (n = 81) | Incidence in the closed primary school peaked on the 3rd day of closure (12 cases) and fell to 2 cases on each of the two following days; no further cases occurred. Incidence in the closed nursery school increased through the first 3 days of closure to a peak of 6 cases, then declined to 0-1 cases per day for 4 days; no further cases occurred after this. Cases in families and friends of the schoolchildren (n = 15) occurred only during the period of school closures. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Poggensee et al (2010) [31] | Outbreak report | General population of Germany, April – November 2009 | Planned holiday. | Duration not stated; school closure is described using the weekly “vacation density” (the percentage of the population living in states in which schools were closed) as the timing of the holiday varied between states | Vacation density peaked in the early stages of the outbreak, while the practice index was below the seasonal threshold and not increasing markedly. A second increase in the vacation density occurred while the practice index was increasing linearly. | Acute respiratory illness reported through sentinel surveillance system, used to calculate a “practice index” (defined as “the relative deviation of observed consultations for ARI divided by all consultations in the same week and set into relation to the background value of this ratio in weeks without influenza virus circulation”) | Practice index remained fairly constant throughout the main school holiday period and increased only when the vacation density was declining; the second increase in the vacation density was followed by a brief plateau in the practice index. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Birrell et al (2011) [32] | Modelling analysis | General population of London, UK, May – December 2009 | Planned holidays | Six week summer holiday and two half terms of one week each (in May and October); all schools in London closed. | As Baguelin et al [28] (closure coincided with peak of the first wave) | Influenza-like illness recorded through GP sentinel surveillance scheme together with serological and virological data; parameters estimated included the reduction in contact rates associated with school holidays. | Both peaks in the two waves of consultations coincided with a school holiday. The summer holiday was estimated to reduce contacts amongst 5-14 year olds by 72% and the half term holiday by 48%; no effects were apparent in other age groups. |
| Evans et al (2011) [33] | Estimation of numbers of ILI cases due to pandemic H1N1 based on GP consultation data, helpline usage, virological swabbing and assumptions about the proportion of infections resulting in healthcare seeking. | General population of England, June – December 2009. | Planned holiday. | Six week summer holiday affecting all schools nationally. | As Baguelin et al [28] (closure coincided with peak of the first wave) | Estimate numbers of ILI cases due to pandemic H1N1, by age and region. | Estimated incidence declined during the school holiday and increased following reopening, in all regions and in all age groups except for the <1 and ≥65 year olds (among whom estimated case numbers were low). |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Smith et al (2011) [34] | Analysis of telephone helpline (NHS Direct) and GP consultation data | General UK population, May – August 2009; results also presented separately for London and West Midlands regions. | Planned school summer holiday (late July to early September). | Approximately six weeks; all schools nationally. | First week of school closure coincided with national peak in NHS Direct calls but occurred after the peak for London and the West Midlands. Consultation data peaked in the first week of closure nationally and before closure in London. | Weekly percentage of calls to NHS Direct that were classified as cold / flu. Weekly GP consultation rates for ILI. | Both indices continued to decline during closure; no data presented after schools reopened. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Flasche et al (2011) [35] | Statistical analysis of relationship between estimated effective reproduction number for H1N1 pandemic influenza in 12 European countries (in 2009) and several explanatory variables, including school holiday dates | General populations in Belgium, Bulgaria, England, France, Germany, Italy, Luxembourg, Netherlands, Portugal, Romania, Slovakia and Spain, April – October 2009. School holidays occurred during the study period in all countries except Bulgaria, England and France. | Planned holidays. | Varied by country. | Varied by country, but typically early in the respective outbreaks. | Effective reproduction number estimated from numbers of laboratory-confirmed pandemic H1N1 infections. | No evidence found of a relationship between the effective reproduction number and the start of school holidays. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| van Gageldonk-Lafeber et al (2011) [36] | Outbreak report; comparison of pandemic and seasonal ILI consultation data. | General population of the Netherlands, and residents of nursing homes considered separately, October – December 2009 | Planned holidays | One week; all schools nationally although timing varied by region. | In north and central regions, schools closed two weeks after the epidemic threshold consultation rate was exceeded nationally; in the south, schools closed one week later. | GP consultation rates for ILI (age-stratified); ILI rates in nursing home residents; age-specific H1N1 hospital admission rates. | Possible reduction in incidence, or slowing of epidemic growth, among 0-4, 5-9, 10-14 and 15-19 year olds; epidemic continued to grow after schools reopened. No apparent effect of school closure on ILI in nursing home residents or hospital admissions. |
| Merler et al (2011) [37] | Modelling analysis of factors influencing spatiotemporal spread of pandemic H1N1 in Europe | General population of 37 European countries, May – December 2009 | Mainly planned holidays; some reactive closures. | Varied by country; summer holidays typically lasted 6-12 weeks and autumn holidays approximately 2 days to 2 weeks. | Varied by country. | Predicted numbers of infections for comparison with ILI surveillance data. | The model reproduced the observed incidence patterns in the different countries most closely when country-specific school holidays were included and contact rates in the population were allowed to change during holidays. (Transmission was assumed to be eliminated in schools and increased by a factor of 1.4 in the community during holidays.) |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Petrovic et al (2011) [38] | Outbreak report / analysis of risk factors for death in hospitalised cases. | Catchment population (n = 102,723) of general practices participating in sentinel surveillance, Vojvodina, Serbia, September 2009 – April 2010. | Response to outbreak. | All schools in Vojvodina; a closure lasting one week was followed six weeks later by a three week closure. | First closure coincided with first peak in ILI consultations in all ages and 5-14 year olds, but after the peak in 0-4 year olds. Second closure occurred after peak. | ILI consultation rates, overall and by age group. | ILI consultation rates declined following first closure and increased after schools reopened, particularly in 5-14 and 15-64 year olds. Rates were already declining when schools closed for second time and continued to do so during closure; possible slight increase after reopening. |
| **Asia** | | | | | | | |
| WHO (2009) [39] | Outbreak report, primarily reporting clinical aspects of infection | School pupils in Hyogo Prefecture and Osaka Prefecture, Japan, May 2009 | Response to school-associated outbreak | 7 days, >1400 schools closed but unclear whether this represents all schools in the two prefectures | Unclear | School absenteeism | No increase in school absenteeism upon reopening of schools (no quantification of absence levels given) |
| Nishiura et al (2009) [40], Shimada et al (2009) [41] | Outbreak reports (both report essentially the same data with slightly different analyses) | General Japanese population, May – June 2009 | Response to outbreak associated primarily with schools; some use of prophylactic oseltamivir [39] | 7 days (possibly more in some cases), all schools in Hyogo and Osaka prefectures (preceded by weekend closure) | First confirmed cases had disease onset on 9 May, weekend / closure began 16 May | Laboratory-confirmed H1N1 influenza (restricted to indigenously-acquired cases in [40] (n = 361[40] or 392 [41]) | Case numbers peaked at ~70 cases on the second day of the weekend, then declined throughout week of closure; no obvious resurgence on reopening |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Kawaguchi et al (2009) [42] | Outbreak report (subset of the data used in the two studies above) | Schools in Osaka Prefecture, Japan, May 2009; ages of affected students not stated. | Response to outbreak; some use of prophylactic oseltamivir in families of cases | 1 week (preceded by a weekend), all 270 high schools and 526 junior high schools, and most nurseries, primary schools, colleges and universities, in Osaka prefecture | Epidemic peaked on second day of closure (i.e. at the weekend) | Confirmed H1N1 infection (n = 156) | Peak of 30 cases on second day of weekend and declined throughout closure period; no resurgence after re-opening |
| Chieochansin et al (2009) [43] | Outbreak report | General population of Bangkok, June – July 2009 | Public holiday followed later by closure in response to outbreak | Public holiday lasted 1 week; schools were subsequently closed for 1 week and tutorial schools for 2 weeks | Public holiday occurred during peak week. Closure of schools and tutorial schools began during the following week. | Laboratory confirmed pandemic H1N1 influenza | Incidence declined throughout period of closure. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Wu et al (2010) [44] | Age-structured SIR model fitted to data on laboratory-confirmed cases during the 2009 pandemic in Hong Kong, used to estimate reporting rates and the reduction in within age group transmission resulting from school closures | General population of Hong Kong, June – August 2009 | Response to outbreak, followed by planned school holiday | All primary schools, kindergartens, childcare centres and special schools closed for ~1 month immediately prior to the summer holiday (duration of holiday not stated). Secondary schools with ≥1 case closed for 14 days, all secondary schools closed for summer holiday at same time as primary schools | At start of growth phase of first wave, which peaked around the 10th day of closure. School holidays started at the beginning of the growth phase of a second wave. | Laboratory-confirmed pandemic influenza cases, proportion of these in different age groups (0-12 years, 13-17 years and ≥18 years) and percentage reduction in within age group transmission resulting from school closures. | First wave continued to grow during school closure, followed by second wave beginning around the start of the school holidays. Following school closure, numbers of cases in 0-12 year olds remained low but the proportion of cases in this age group increased slightly, while that in 13-17 year olds decreased. School closure was estimated to reduce transmission between children of the relevant age group by 70% (95% CI 64-75%), corresponding to an overall reduction in transmission of ~25%. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Cowling et al (2010) [45] | Modelling analysis | General population of Hong Kong, May – October 2009 | Response to outbreak, followed by planned school holiday | All primary schools, kindergartens, childcare centres and special schools closed for ~1 month immediately prior to the summer holiday (duration of holiday not stated). Secondary schools with ≥1 case closed for 14 days, all secondary schools closed for summer holiday at same time as primary schools | At start of growth phase of first wave, which peaked around the 10th day of closure. School holidays started at the beginning of the growth phase of a second wave. | Laboratory-confirmed pandemic influenza cases and hospitalisations, used to estimate daily values of the effective reproduction number. | Effective reproduction number declined during initial days of closure, oscillated around 1 for the duration of the closure period, increased very slightly when schools reopened before declining again. |
| Hsueh et al (2010) [46] | Outbreak report | General population of Taipei City, Taiwan, June 2009 – January 2010 | Response to outbreak | Individual classes suspended for at least 5 days if >2 students had confirmed infection within 3 days. | Timing for individual schools not presented; number of class suspensions generally increased with the number of hospitalisations. | Hospitalisations with pandemic H1N1. | Number of class suspensions generally followed the number of hospitalisations. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Wu et al (2010) [47] | Vaccine study amongst children attending public primary and middle schools and participating in a national celebration parade. | 95244 vaccinated participants in a national celebration parade, Beijing; of these, 25037 vaccinated schoolchildren were compared to 244091 unvaccinated schoolchildren. | Planned national holiday | 1 week, all schools nationally. | Schools closed as cumulative incidence in unvaccinated students began to plateau | Laboratory confirmed H1N1 infection | Cumulative incidence in unvaccinated children increased very slightly during the school closure (from ~220 to ~260 per 100,000); rate of increase in cumulative incidence increased ~1 week after schools reopened. Cumulative incidence in vaccinated students remained relatively constant before, during and after school closure. |
| Huai et al (2010) [48] | Outbreak report | Primary school (1314 pupils) in Dongguan City, Guangdong Province, China, June 2009 | Response to outbreak, shortly followed by planned summer break. | Affected primary school closed 19-28 June; all schools in the town closed 22-28 June, Planned summer break began on 2 July. | Affected school closed on day of peak. | Confirmed or suspected cases in children attending affected school (n = 105); limited data on cases in the community are also included. | Epidemic in schoolchildren peaked at 30 cases on the first day of closure, declining to 11 the following day. No further cases occurred between the last two days of closure and the subsequent closure for the holiday. |
| Engelhard et al (2011) [49] | Outbreak report | Children aged <18 years enrolled with one health maintenance organisation in Israel, June 2009 – April 2010. | Two separate planned holidays. | Summer holiday lasted 9 weeks, autumn holiday lasted 5 weeks. | Summer holiday occurred close to beginning of first wave; autumn holiday close to beginning of second. | Rate of ILI (fever with one or more of cough, coryza, sore throat, myalgia) visits to community health clinics. | ILI rate peaked and decliend during summer holiday, began to increase when schools reopened and reached a second peak during the autumn holiday before declining again. A third wave occurred after the autumn holiday. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Leung et al (2011) [50] | Outbreak report / analysis of household secondary attack rates and effect of oseltamivir. | 511 children attending a secondary school in Hong Kong and their 205 household contacts, June 2009. No cases occurred amongst the 153 school staff. | Response to outbreak | Two weeks, coinciding with closure of all schools in Hong Kong. | Three days after peak. | Laboratory-confirmed pandemic H1N1 in schoolchildren or household contacts. | Incidence increased during first two days of closure and subsequently remained very low; last case occurred one week before reopening. |
| Uchida et al (2011) [51] | Prospective study of pandemic H1N1 | 2318 schoolchildren, 11424 university students and 3344 staff members associated with Shinshu University Organisation, August 2009 – March 2010 | Planned breaks and reactive closures. | Planned summer holiday affected all schools for approximately one month; winter holiday for 3 weeks; reactive school and class closures varied for individual schools. | Summer holiday occurred before outbreak began; winter holiday occurred while incidence was declining. Timing of reactive closures in relation to incidence in individual schools unclear. | "Influenza-like symptoms and diagnosed with confirmed, probable or suspected swine flu at hospital or clinics." | Incidence continued to decline during the winter holiday. Incidence also appeared to declined during reactive school and class closures, but this is unclear as data are not presented for individual schools. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| **Africa** | | | | | | | |
| Rajatonirina et al (2011) [52] | Outbreak report / analysis of oseltamivir compliance and side effects. | 132 boarders at a school in Antananarivo, Madagascar, October – November 2009. | Planned holiday | 2 weeks | After main phase of epidemic. | At least one influenza-like symptom (n = 56 with known onset date). | Epidemic appeared to be largely over when the school closed; sporadic cases continued to occur during closure period. |
| **Australasia** | | | | | | | |
| Caley et al (2008) [53] | Transmission modelling analysis of hospitalisation and mortality data | Sydney, 1919 (all ages) | Response to outbreak; combined with other social distancing interventions | ~4.5 weeks initially; schools reopened for ~3 weeks and then closed for a further ~2 months. | Initial closure occurred as first cases were detected; second closure occurred during exponential growth phase of epidemic. | Estimated reduction in “behaviours resulting in disease transmission.” | Transmission reduced by 38% during period of school closure. |
| Baker et al (2009) [54] | Outbreak report | New Zealand population, April – August 2009 (all ages) | Planned national holiday during national outbreak; some use of prophylactic antivirals during containment phase [55] | 2 weeks, apparently all schools nationally | Depending on indicator, closure coincided with peak, preceded it by 1 week, or followed it by 1-3 weeks | Cases reported through notifiable disease surveillance system (n = 3179); hospitalisations amongst these cases (n = 972); ICU influenza admissions (n = 106); GP consultation rates (two surveillance systems) | Notifications, hospitalisations and ICU admissions began to decline during second week of closure. GP consultation rates for 5-14 year olds increased following re-opening (in one of the systems only). |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Effler et al (2010) [56] | Outbreak report focussing on children's activities during closure and the effects of closure on families | Three schools in Perth, Western Australia, May – July 2009; ages of affected pupils not stated. Data available for 233 of 402 students. | Response to outbreak | 1 week; one school closed completely and two closed only affected year groups | Confirmed cases in individuals attending the three schools peaked two days before closure | Confirmed pandemic H1N1 infection | Confirmed cases peaked at ~9/day two days before closure, subsequently a maximum of 1 case / day occurred. |
| Paine et al (2010) [57] | Outbreak report and modelling analysis | New Zealand population, April – November 2009 (all ages) | Planned national holiday during national outbreak; some use of prophylactic antivirals during containment phase [55] | 2 weeks, all schools nationally | ~4 days before peak. | Cases reported through notifiable disease surveillance system (n = 3254), used to estimate daily values of the effective reproduction number | Case numbers peaked and declined during holiday, no consistent increase when schools reopened. Effective reproduction number was declining before school closure and continued to decrease during the holiday, appeared to increase slightly and reach a plateau after schools reopened. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| **Americas** | | | | | | | |
| Cruz-Pacheco et al (2009) [58] | Estimation of contact rates based on estimated values of $R_0$ before and after introduction of control measures | Mexico City, April – May 2009 (all ages) | Response to outbreak; no use of antivirals | ~2.5 weeks, all schools in Mexico City. | Epidemic had been growing exponentially for ~1 week when schools were closed | Number of confirmed (n = 1752) or probable (n = 6114) cases; estimated daily reproduction number ($R_t$) | Incidence increased initially to peak of ~400 probable and 150 confirmed cases/day on second and third days of closure, then declined gradually over the closure period. $R_t$ declined from ~1.6 before and during the closure, crossing 1 within 2 days of closure and remaining <1 thereafter. |
| Echevarria-Zuno et al (2009) [59] | Outbreak report | National population of Mexico, April – July 2009 | Response to outbreak; no mention of antiviral prophylaxis | Approx two weeks; entire education system (including nurseries and universities) initially in Mexico City and Mexico State from 23 April, then nationwide from 27 April [60]. Universities and high schools reopened 4-5 days before elementary schools [58]. | Schools closed early in growth phase of epidemic. | ILI reported through active surveillance of inpatients and outpatients | Epidemic continued while schools were closed and peaked ~1 week after closure; increase in cases over three days after reopening of universities and high schools, but not following subsequent reopening of elementary schools. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Lajous et al (2010) [61] | Outbreak report | 56,551 respondents to a text message survey, Mexico, April 2009 | Both planned closure and a response to the outbreak | Planned holiday lasted 1 week; reactive closure lasted at least one week (schools were still closed at the end of the time period presented) | Planned closure occurred in the early stages of the outbreak before national surveillance indicated an increase in the number of cases but case numbers from survey data were declining. Reactive closure occurred during the increase in national case numbers. | ILI in survey respondents; suspected or confirmed H1N1 from national surveillance | Planned closure was followed by a slight decrease in case numbers reported through national surveillance, but this increased before schools reopened. National surveillance data peaked ~3 days after the reactive school closure and then declined through the rest of the closure period. Survey data were not obviously affected by school closure, although the proportion of reported cases which prevented respondents working declined during both closure periods. |
| Gomez et al (2009) [62] | Outbreak report | National population of Peru, May – September 2009 | Appears to be reactive, but unclear; some use of prophylactic oseltamivir | 3 weeks, all schools nationwide | One week after peak week | Number of pneumonia cases in 5-59 year olds in Lima and Callao; number of severe acute respiratory infections nationally | Pneumonia cases decreased from peak week ~130 cases following closure to ~40 cases and showed slight resurgence to just below 60 cases when schools re-opened; effect on other severe respiratory infections difficult to assess as date of closure is unclear. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Tinoco et al (2009) [63] | Prospective cohort study | 1747 individuals in 343 randomly selected households, San Juan de Miraflores District, Lima, Peru, May – August 2009 | Unclear | ~3 weeks, presumably all schools | After peak | Influenza-like illness counts by causative organism (H1N1 or other); age-specific rates of confirmed H1N1v | Number of ILI cases (and confirmed H1N1) decreased throughout closure period, from 54 (39 H1N1) the preceding week to 29 (19), 12 (6) and 6 (3) in each subsequent week; rates of confirmed H1N1 reached zero in week following closure in all age groups except 50-59 year olds. |
| Lessler et al (2009) [64] | Outbreak report | 1453 students (aged 14-19) and staff at a New York City high school, April – May 2009 | Response to outbreak | 9 days, one school | After peak | Confirmed H1N1 influenza or self-reported ILI | Incidence already declining when school was closed, continued to decline through closure period. No data presented for period following re-opening. |
| Miller et al (2010) [65] | Survey of schoolchildren regarding behaviour during reactive school closure | Private girls' school in Boston, USA; 63 of 176 children in grades 5-8 and 188 of 240 in grades 9-12. | Response to outbreak / high levels of absenteeism | One week | 4 days after peak | Fever in pupils with ILI, and absenteeism, in upper and lower school separately | Upper and lower schools each had one case of fever on the first day of closure and continued to have 0 or 1 case per day throughout the closure period; no apparent increase on reopening. Absenteeism in both schools was considerably higher before closure than after reopening. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Janjua et al (2010) [66] | Telephone survey of households of children enrolled in any of the six schools in the community, primarily aimed at conducting a case-control study of the effect of vaccination against seasonal influenza on risk of infection with pandemic H1N1. | Elementary school and surrounding community, British Colombia, Canada, April – May 2009. | Response to outbreak in one elementary school | 9 days | Outbreak peaked on the first day of school closure | ILI (n = 92) in 1092 participants from households of children attending any school in the community | Daily number of cases declined during school closure (from 10 cases on the first day to 1 case on the final day), increasing to 5 cases on the day of reopening. Case numbers ranged from 0-3 per day for the remainder of the study period. |
| Marchbanks et al (2011) [67] | Outbreak report | 388 of 456 pupils at an elementary school in Pennsylvania, USA, and 957 household contacts, May 2009. | Response to outbreak | 7 days | ILI peaked two days before school closure. | ILI (93 pupils and 74 contacts): subjective fever with cough and / or sore throat. | Incidence increased on second day of closure and then declined; very slight increase on reopening (although absenteeism returned to normal). No cases occurredin the 4th grade during closure or after reopening. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Cauchemez et al (2011) [68] | More detailed modelling analysis of outbreak described in Marchbanks et al [67] | Same school as Marchbanks et al [67], but using data from 27 April to 30 May 2009 from 370 pupils and 899 household contacts. | As Marchbanks et al [67] | As Marchbanks et al [67] | ARI epidemic curve peaked 2 and 3 days before closure. | Acute respiratory infection (at least two of fever, cough, sore throat, runny nose) in children attending the affected school (stratified by grade) and their household contacts (stratified into adults and children).129 cases in pupils and 141 in household contacts. | Incidence increased on the second day of closure but then declined; slight increase on reopening. Statistical analysis found no evidence of an effect of closure on the transmission rate among pupils (30% reduction, 95% credible interval 62% decrease to 22% increase). Reproduction number was also similar (0.3) during the week of closure and the following week. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Janusz et al (2011) [69] | Outbreak report and community-based survey. Community survey collected data from 240 of 711 households approached (comprising 644 individuals). | A community associated with a school which experienced an outbreak, Chicago, USA, April – May 2009. | Response to outbreak. | 7 days; one of the five elementary schools in the community closed. | Approximately one third of ILI cases reported through the survey had occurred before school closure (0-3 per day). Only 4 laboratory-confirmed cases had been reported to the Department of Health before closure. | ILI (fever with cough and / or sore throat, n = 37) in the survey; laboratory confirmed H1N1 infection reported to Chicago Department of Public Health (n = 43) based on date of specimen collection, although the peak based on date of onset occurred 3 days before closure. | In the community survey, maximum of 3 cases per day before and during closure; no increase when school reopened. None of the cases reported through this survey were linked to the affected school.<br><br>Laboratory reports peaked on the first day of closure, generally declined during closure and remained low after reopening; however, testing recommendations changed on the second day of closure. |
| Cohen et al (2011) [70] | Outbreak report | Pupils at a school in Chicago which closed due to the outbreak, and their household contacts (170 households, of 609 eligible, provided data), April – May 2009. | Response to outbreak. | 1 week. | Highest numbers of cases were reported on the two days before closure. | Acute respiratory illness (one or more of fever, cough, sore throat, rhinorrhoea or nasal congestion, n = 58). | Case numbers were lower on the first day of closure than on the two previous days, increased during closure and then declined. Few cases were reported after school reopened. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Loustalot et al (2011) [71] | Questionnaire survey / assessment of household secondary attack rate and use of non-pharmaceutical interventions. | 668 households (2772 individuals) of 1716 approached, with children attending a closed high school in San Antonio, Texas, March – June 2009. | Response to outbreak | 9 days | Peak occurred 8 days before school closure | ILI in household members reported by one adult household member, stratified into index cases (students attending the affected school, n = 78) and secondary cases (n = 21) | Incidence remained low during closure; no cases reported on the final four days of closure. 1-2 cases per day after school reopened. |
| Chowell et al (2011a) [72] | Epidemiological and modelling analysis of outbreak data | 107 million individuals registered with a Mexican private medical system, April – December 2009 | Response to outbreak, and a later planned summer holiday. | Reactive closure lasted from 24 April to 5 May; summer holiday lasted ~7 weeks; all schools nationally were closed. | Reactive closure occurred early in the first wave of the outbreak (together with other interventions); summer holiday followed a plateau in the number of confirmed cases. | Confirmed pandemic H1N1 cases or ratio of number of cases in students (aged 5-20 years) to number of cases in other age groups. | Reactive closure appeared to slow epidemic growth, which resumed when interventions were lifted. Incidence was reasonably constant in all ages during the summer holiday but declined amongst students; cases amongst students and others increased when schools reopened (as did the ratio of student to non-student cases). |
| Herrera-Valdez et al (2011) [73] | Modelling analysis, including estimation of change in contact rate during school closure period. | National population of Mexico, April – November 2009 | One reactive closure and a subsequent planned holiday | Reactive closure lasted ~2 weeks; holiday lasted ~2 months. | Schools closed reactively early in growth phase; holiday started close to the peak of the second wave. | Confirmed pandemic H1N1 cases; model estimates of contact rate. | Confirmed cases occurred in three waves corresponding to closing and reopening of schools. Estimated contact rates appeared to be reduced by ~80% during school closure periods. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Chowell et al (2011b) [74] | Epidemiological / spatial analysis of outbreak data | General population of Peru, May – December 2009 | Planned school holiday moved forward by two weeks | Three weeks, all schools in the country | After the peak in daily national data; same week as peak in weekly data stratified into students and others. | Confirmed pandemic H1N1 cases or ratio of number of cases in students (aged 5-20 years) to number of cases in other age groups. | Number of cases in whole population, students and others declined throughout closure period; no clear increase on reopening. Ratio of student to non-student cases had already peaked, but declined during closure and increased afterwards. |
| Monto et al (1970) [75] | Non-randomised community trial of pandemic vaccine | All schoolchildren in Tecumseh (approx 3680) and Adrian (number not stated), Michigan, November 1968 – January 1969. 86% of children and a small number of adults in Tecumseh were vaccinated against the pandemic strain. Pandemic vaccine was not used in Adrian. | Christmas holiday | Two weeks, presumably all schools | Peak absenteeism in Adrian occurred one week before closure; Tecumseh did not experience an extensive epidemic. | School absenteeism (all causes) | Absenteeism in Adrian was >14% on each of the four days before closure and was ~8% on the day of reopening. Tecumseh did not experience any clear peaks in absenteeism. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Bootsma and Ferguson (2007) [76] | Statistical / transmission modelling analysis of historical P&I mortality data | 23 US cities with data on timing of introduction of NPIs during 1918 influenza pandemic | Response to outbreaks; other social distancing measures also implemented | Approx 0-7 weeks, depending on city | Varied by city | Excess total or peak mortality in each city | Correlation between excess / peak mortality and timing of introduction of NPIs relative to progress of epidemic ($p<0.01$ in both cases). Lifting of NPIs allowed transmission to become established again |
| Hatchett et al (2007) [77] | Statistical analysis of historical P&I mortality data | 17 US cities, September – December 1918 | Response to outbreaks; other social distancing measures also implemented | Varied by city | Varied by city | Cumulative Excess P&I death rates (CEPID) | Cities which closed schools before CEPID reached 30/100,000 had a lower median peak weekly excess P&I death rate than those which did not ($p<0.01$) but there was no significant difference in median CEPID. Closing schools at a higher CEPID was associated with higher peak P&I death rates (Spearman $\rho$ =0.54) but not with total P&I death rates. Second waves occurred only after lifting of NPIs. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Markel et al (2007) [78] | Statistical analysis of historical mortality data | 43 US cities, September 1918 – February 1919 | Response to outbreaks; other social distancing measures also implemented | Varied by city | Varied by city | Weekly excess P&I death rates | Not uniform across cities (but this could be related to the timing of the intervention). Earlier interventions correlated with increased time to epidemic peak (r = -0.74, p<0.001), reduced peak excess death rate (r = 0.31, p=0.02) and reduced total excess death rate (r = 0.37, p=0.008). Increased duration of intervention associated with reduced total excess death rate (r = -0.39, p=0.005). |
| Jordan et al (1919) [79] | Outbreak report | Elementary school (391 pupils aged 4-13 years) and high school (427 pupils aged 14-18 years) of University of Chicago, October – December 1918 | Planned Thanksgiving break | Four days (including weekend) | Both schools were closed for final three days of peak week and one day of the following week. | Clinical influenza (n = 97 in elementary school, n = 91 in high school) | Elementary school: incidence declined from 19 cases in peak week to 15 the following week, showed a second peak of 10 cases 3 weeks after the closure. High school: incidence decreased from 16 cases in peak week to 5 the following week, showed a second peak of 11 cases 2 weeks after the closure. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Armstrong and Hopkins (1921) [80] | Outbreak report | Kelleys Island, Lake Erie, US, January – February 1920, population 689 (of whom 157 were schoolchildren) | Response to staff and student absenteeism during influenza outbreak | The single school (for both grammar and high school pupils) on the island remained closed "until the epidemic had subsided" | Epidemic began 24 January, school closed 30 January | Self-reported clinical influenza, based on checklist of symptoms ( n = 369) | Overall incidence peaked at 52 cases on day following closure. Cases in schoolchildren dipped on day of closure, peaked following day and declined thereafter. Cases in other groups dipped two days after closure, peaked the following day and then declined. |
| Winslow and Rogers (1920) [81] | Outbreak report | Connecticut, USA, September – December 1918 | Response to outbreak | Three cities in which schools remained open are cited and mortality rates compared descriptively with two cities in which schools were closed. Duration of closures not stated. | Not stated. | Deaths from pneumonia and influenza | Death rates were lower in the three cities in which schools remained open than in at least two cities in which they were closed. |

## Supplementary references


1. Briscoe JH. The protective effect of influenza vaccine in a mixed influenza A and B epidemic in a boys' boarding school. *J R Coll Gen Pract* 1977;27(166):28-31.
2. Davies JR, Grilli EA, Smith AJ, Hoskins TW. Prophylactic use of amantadine in a boarding school outbreak of influenza A. *J R Coll Gen Pract* 1988;38(313):346-8.
3. Grilli EA, Anderson MJ, Hoskins TW. Concurrent outbreaks of influenza and parvovirus B19 in a boys' boarding school. *Epidemiology and Infection* 1989;103(2):359-69.
4. Danis K, Fitzgerald M, Connell J, Conlon M, Murphy PG. Lessons from a pre-season influenza outbreak in a day school. *Commun Dis Public Health* 2004;7(3):179-83.
5. Miller DL, Lee JA. Influenza in Britain 1967-68. *Journal of Hygiene* 1969;67:559-72.
6. Cauchemez S, Valleron A-J, Boelle P-Y, Flahault A, Ferguson NM. Estimating the impact of school closure on influenza transmission from Sentinel data. *Nature* 2008;452(7188):750-4.
7. Olson JG. School absenteeism during an outbread of B/Hong Kong/5/72-like influenze virus in Taipei, Taiwan. *Southeast Asian J Trop Med Public Health* 1980;11(4):429-34.
8. Sonoguchi T, Naito H, Hara M. Cross-subtype protection in humans during sequential, overlapping, and/or concurrent epidemics caused by H3N2 and H1N1 influenza viruses. *Journal of Infectious Diseases* 1985;151(1):81-88.
9. Fujii H, Takahashi H, Ohyama T, Hattori K, Suzuki S. Evaluation of the school health surveillance system for influenza, Tokyo, 1999-2000. *Japanese Journal of Infectious Diseases* 2002;55(3):97-98.
10. Heymann A, Chodick G, Reichman B, Kokia E, Laufer J. Influence of school closure on the incidence of viral respiratory diseases among children and on health care utilization. *Pediatr Infect Dis J* 2004;23(7):675-7.
11. Heymann AD, Hoch I, Valinsky L, Kokia E, Steinberg DM. School closure may be effective in reducing transmission of respiratory viruses in the community. *Epidemiol Infect* 2009;137(10):1369-76.
12. Lo JY, Tsang TH, Leung YH, Yeung EY, Wu T, Lim WW. Respiratory infections during SARS outbreak, Hong Kong, 2003. *Emerg Infect Dis* 2005;11(11):1738-41.
13. Cowling BJ, Lau EHY, Lam CLH, Cheng CKY, Kovar J, Chan KH, et al. Effects of school closures, 2008 winter influenza season, Hong Kong. *Emerg Infect Dis* 2008;14(10):1660-2.
14. Cashman P, Massey P, Durrheim D, Islam F, Merritt T, Eastwood K. Pneumonia cluster in a boarding school--implications for influenza control. *Commun Dis Intell* 2007;31(3):296-8.
15. Shaw C, McLean M, McKenzie J. Other surveillance reports: influenza-like illness in Wellington schools 2005. *New Zealand Public Health Surveillance Report* 2006;4(2):4-6.
16. Leonida DDJ. Morbidity patterns reflected in a school health program during an influenza epidemic season. *Illinois Medical Journal* 1970;137(3):262-64.
17. Glass RI, Brann EA, Slade JD, Jones WE, Scally MJ, Craven RB, et al. Community-wide surveillance of influenza after outbreaks due to H3N2 (A/Victoria/75 and A/Texas/77) and H1N1 (A/USSR/77) influenza viruses, Mercer County, New Jersey, 1978. *Journal of Infectious Diseases* 1978;138(5):703-6.
18. Farley TA, St. Germain JM, Chamberlain LA, Krassner L. The impact of influenza vaccination on respiratory illness at a boarding School. *Journal of American College Health* 1992;41(3):127-31.

19. Louie JK, Schnurr DP, Guevara HF, Honarmand S, Cheung M, Cottam D, et al. Creating a Model Program for Influenza Surveillance in California. Results from the 2005-2006 Influenza Season. *American Journal of Preventive Medicine* 2007;33(4):353-57.
20. Johnson AJ, Moore ZS, Edelson PJ, Kinnane L, Davies M, Shay DK, et al. Household responses to school closure resulting from outbreak of influenza B, North Carolina. *Emerg Infect Dis* 2008;14(7):1024-30.
21. Rodriguez CV, Rietberg K, Baer A, Kwan-Gett T, Duchin J. Association between school closure and subsequent absenteeism during a seasonal influenza epidemic. *Epidemiology* 2009;20(6):787-92.
22. Wheeler CC, Erhart LM, Jehn ML. Effect of school closure on the incidence of influenza among school-age children in Arizona. *Public Health Rep* 2010;125(6):851-9.
23. Smith A, Coles S, Johnson S, Saldana L, Ihekweazu C, O'Moore E. An outbreak of influenza A(H1N1)v in a boarding school in South East England, May-June 2009. *Euro Surveill* 2009;14(27):9.
24. Health Protection Agency West Midlands H1N1v Investigation Team. Preliminary descriptive epidemiology of a large school outbreak of influenza A(H1N1)v in the West Midlands, United Kingdom, May 2009. *Euro Surveill* 2009;14(27).
25. Wallensten A, Oliver I, Lewis D, Harrison S. Compliance and side effects of prophylactic oseltamivir treatment in a school in South West England. *Euro Surveill* 2009;14(30):19285.
26. Calatayud L, Kurkela S, Neave PE, Brock A, Perkins S, Zuckerman M, et al. Pandemic (H1N1) 2009 virus outbreak in a school in London, April-May 2009: an observational study. *Epidemiol Infect* 2010;138(2):183-91.
27. Strong M, Burrows J, Stedman E, Redgrave P. Adverse drug effects following oseltamivir mass treatment and prophylaxis in a school outbreak of 2009 pandemic influenza A(H1N1) in June 2009, Sheffield, United Kingdom. *Euro Surveill* 2010;15(19):pii/19565.
28. Baguelin M, Hoek AJV, Jit M, Flasche S, White PJ, Edmunds WJ. Vaccination against pandemic influenza A/H1N1v in England: A real-time economic evaluation. *Vaccine* 2010;28(12):2370-84.
29. Guinard A, Grout L, Durand C, Schwoebel V. Outbreak of influenza A(H1N1)v without travel history in a school in the Toulouse district, France, June 2009. *Euro Surveill* 2009;14(27).
30. Carrillo-Santisteve P, Renard-Dubois S, Cheron G, Csaszar-Goutchkoff M, Lecuit M, Lortholary O, et al. 2009 pandemic influenza A(H1N1) outbreak in a complex of schools in Paris, France, June 2009. *Euro Surveill* 2010;15(25):24.
31. Poggensee G, Gilsdorf A, Buda S, Eckmanns T, Claus H, Altmann D, et al. The first wave of pandemic influenza (H1N1) 2009 in Germany: From initiation to acceleration. *BMC Infectious Diseases* 2010;10(155).
32. Birrell PJ, Ketsetzis G, Gay NJ, Cooper BS, Presanis AM, Harris RJ, et al. Bayesian modeling to unmask and predict influenza A/H1N1pdm dynamics in London. *Proceedings of the National Academy of Sciences of the United States of America* 2011;108(45):18238-43.
33. Evans B, Charlett A, Powers C, McLean E, Zhao H, Bermingham A, et al. Has estimation of numbers of cases of pandemic influenza H1N1 in England in 2009 provided a useful measure of the occurrence of disease? *Influenza and other Respiratory Viruses* 2011;5(6):e504-e12.
34. Smith S, Smith GE, Olowokure B, Ibbotson S, Foord D, Maguire H, et al. Early spread of the 2009 infuenza A(H1N1) pandemic in the United Kingdom - use of local syndromic data, May-August 2009. *Eurosurveillance* 2011;16(3).

35. Flasche S, Hens N, Boëlle P-Y, Mossong J, van Ballegooijen WM, Nunes B, et al. Different transmission patterns in the early stages of the influenza A(H1N1)v pandemic: A comparative analysis of 12 European countries. *Epidemics* 2011;3(2):125-33.
36. Van Gageldonk-Lafeber AB, Hooiveld M, Meijer A, Donker GA, Veldman-Ariesen MJ, van der Hoek W, et al. The relative clinical impact of 2009 pandemic influenza A (H1N1) in the community compared to seasonal influenza in the Netherlands was most marked among 5-14year olds. *Influenza and other Respiratory Viruses* 2011;5(6):e513-e20.
37. Merler S, Ajelli M, Pugliese A, Ferguson NM. Determinants of the spatiotemporal dynamics of the 2009 H1N1 pandemic in europe: Implications for real-time modelling. *PLoS Computational Biology* 2011;7(9).
38. Petrovic V, Seguljev Z, Cosic G, Ristic M, Nedeljkovic J, Dragnic N, et al. Overview of the winter wave of 2009 pandemic influenza A(H1N1)v in Vojvodina, Serbia. *Croatian Medical Journal* 2011;52(2):141-50.
39. Human infection with new influenza A (H1N1) virus: clinical observations from a school-associated outbreak in Kobe, Japan, May 2009. *Wkly Epidemiol Rec* 2009;84(24):237-44.
40. Nishiura H, Castillo-Chavez C, Safan M, Chowell G. Transmission potential of the new influenza A(H1N1) virus and its age-specificity in Japan. *Euro Surveill* 2009;14(22):4.
41. Shimada T, Gu Y, Kamiya H, Komiya N, Odaira F, Sunagawa T, et al. Epidemiology of influenza A(H1N1)v virus infection in Japan, May-June 2009. *Euro Surveill* 2009;14(24).
42. Kawaguchi R, Miyazono M, Noda T, Takayama Y, Sasai Y, Iso H. Influenza (H1N1) 2009 outbreak and school closure, Osaka Prefecture, Japan. *Emerg Infect Dis* 2009;15(10):1685.
43. Chieochansin T, Makkoch J, Suwannakarn K, Payungporn S, Poovorawan Y. Novel H1N1 2009 influenza virus infection in Bangkok, Thailand:Effects of school closures. *Asian Biomedicine* 2009;3(5):469-75.
44. Wu JT, Cowling BJ, Lau EH, Ip DK, Ho LM, Tsang T, et al. School closure and mitigation of pandemic (H1N1) 2009, Hong Kong. *Emerg Infect Dis* 2010;16(3):538-41.
45. Cowling BJ, Lau MSY, Ho LM, Chuang SK, Tsang T, Liu SH, et al. The effective reproduction number of pandemic influenza: Prospective estimation. *Epidemiology* 2010;21(6):842-46.
46. Hsueh P-R, Lee P-I, Hsiang Chiu A-W, Yen M-Y. Pandemic (H1N1) 2009 vaccination and class suspensions after outbreaks, Taipei City, Taiwan. *Emerg Infect Dis* 2010;16(8):1309-11.
47. Wu J, Xu F, Lu L, Lu M, Miao L, Gao T, et al. Safety and effectiveness of a 2009 H1N1 vaccine in Beijing. *New England Journal of Medicine* 2010;363(25):2416-23.
48. Huai Y, Lin J, Varma JK, Peng Z, He J, Cheng C, et al. A primary school outbreak of pandemic 2009 influenza A (H1N1) in China. *Influenza other respi* 2010;4(5):259-66.
49. Engelhard D, Bromberg M, Averbuch D, Tenenbaum A, Goldmann D, Kunin M, et al. Increased extent of and risk factors for pandemic (H1N1) 2009 and seasonal infl uenza among children, Israel. *Emerging Infectious Diseases* 2011;17(9):1740-43.
50. Leung YH, Li MP, Chuang SK. A school outbreak of pandemic (H1N1) 2009 infection: assessment of secondary household transmission and the protective role of oseltamivir. *Epidemiol Infect* 2011;139(1):41-4.

51. Uchida M, Tsukahara T, Kaneko M, Washizuka S, Kawa S. Swine-origin influenza a outbreak 2009 at Shinshu University, Japan. *BMC Public Health* 2011;11:79.
52. Rajatonirina S, Heraud J-M, Randrianasolo L, Razanajatovo N, Ramandimbisoa T, Ratsitorahina M, et al. Pandemic influenza A(H1N1) 2009 virus outbreak among boarding school pupils in Madagascar: compliance and adverse effects of prophylactic oseltamivir treatment. *J* 2011;5(3):156-62.
53. Caley P, Philp DJ, McCracken K. Quantifying social distancing arising from pandemic influenza. *Journal of the Royal Society Interface* 2008;5(23):631-9.
54. Baker MG, Wilson N, Huang QS, Paine S, Lopez L, Bandaranayake D, et al. Pandemic influenza A(H1N1)v in New Zealand: the experience from April to August 2009. *Euro Surveill* 2009;14(34).
55. Hall RJ, Peacey MP, Ralston JC, Bocacao J, Ziki M, Gunn W, et al. Pandemic influenza A(H1N1)v viruses currently circulating in New Zealand are sensitive to oseltamivir. *Euro Surveill* 2009;14(30):19282.
56. Effler PV, Carcione D, Giele C, Dowse GK, Goggin L, Mak DB. Household responses to pandemic (H1N1) 2009-related school closures, Perth, Western Australia. *Emerg Infect Dis* 2010;16(2):205-11.
57. Paine S, Mercer GN, Kelly PM, Bandaranayake D, Baker MG, Huang QS, et al. Transmissibility of 2009 pandemic influenza A(H1N1) in New Zealand: effective reproduction number and influence of age, ethnicity and importations. *Euro Surveill* 2010;15(24).
58. Cruz-Pacheco G, Duran L, Esteva L, Minzoni A, Lopez-Cervantes M, Panayotaros P, et al. Modelling of the influenza A(H1N1)v outbreak in Mexico City, April-May 2009, with control sanitary measures. *Euro Surveill* 2009;14(26).
59. Echevarria-Zuno S, Mejia-Arangure JM, Mar-Obeso AJ, Grajales-Muniz C, Robles-Perez E, Gonzalez-Leon M, et al. Infection and death from influenza A H1N1 virus in Mexico: a retrospective analysis. *Lancet* 2009.
60. Stern AM, Markel H. What Mexico taught the world about pandemic influenza preparedness and community mitigation strategies. *Jama* 2009;302(11):1221-2.
61. Lajous M, Danon L, Lopez-Ridaura R, Astley CM, Miller JC, Dowell SF, et al. Mobile messaging as surveillance tool during pandemic (H1N1) 2009, Mexico. *Emerg Infect Dis* 2010;16(9):1488-9.
62. Gomez J, Munayco C, Arrasco J, Suarez L, Laguna-Torres V, Aguilar P, et al. Pandemic influenza in a southern hemisphere setting: the experience in Peru from May to September, 2009. *Euro Surveill* 2009;14(42).
63. Tinoco Y, Razuri H, Ortiz EJ, Gomez J, Widdowson MA, Uyeki T, et al. Preliminary population-based epidemiological and clinical data on 2009 pandemic H1N1 influenza A (pH1N1) from Lima, Peru. *Influenza Other Respi Viruses* 2009;3(6):253-6.
64. Lessler J, Reich NG, Cummings DAT, New York City Department of H, Mental Hygiene Swine Influenza Investigation T, Nair HP, et al. Outbreak of 2009 pandemic influenza A (H1N1) at a New York City school. *N Engl J Med* 2009;361(27):2628-36.
65. Miller JC, Danon L, O'Hagan JJ, Goldstein E, Lajous M, Lipsitch M. Student behavior during a school closure caused by pandemic influenza A/H1N1. *PLoS ONE* 2010;5(5):e10425.
66. Janjua NZ, Skowronski DM, Hottes TS, Osei W, Adams E, Petric M, et al. Seasonal influenza vaccine and increased risk of pandemic A/H1N1-related illness: First detection of the association in British Columbia, Canada. *Clinical Infectious Diseases* 2010;51(9):1017-27.

67. Marchbanks TL, Bhattarai A, Fagan RP, Ostroff S, Sodha SV, Moll ME, et al. An outbreak of 2009 pandemic influenza A (H1N1) virus infection in an elementary school in Pennsylvania. *Clin Infect Dis* 2011;52 Suppl 1:S154-60.
68. Cauchemez S, Bhattarai A, Marchbanks TL, Fagan RP, Ostroff S, Ferguson NM, et al. Role of social networks in shaping disease transmission during a community outbreak of 2009 H1N1 pandemic influenza. *Proc Natl Acad Sci U S A* 2011;108(7):2825-30.
69. Janusz KB, Cortes JE, Serdarevic F, Jones RC, Jones JD, Ritger KA, et al. Influenza-like illness in a community surrounding a school-based outbreak of 2009 pandemic influenza A (H1N1) virus-Chicago, Illinois, 2009. *Clin Infect Dis* 2011;52 Suppl 1:S94-101.
70. Cohen NJ, Callahan DB, Gonzalez V, Balaban V, Wang RT, Pordell P, et al. Respiratory illness in households of school-dismissed students during pandemic (H1N1) 2009. *Emerging Infectious Diseases* 2011;17(9):1756-57.
71. Loustalot F, Silk BJ, Gaither A, Shim T, Lamias M, Dawood F, et al. Household transmission of 2009 pandemic influenza A (H1N1) and nonpharmaceutical interventions among households of high school students in San Antonio, Texas. *Clin Infect Dis* 2011;52 Suppl 1:S146-53.
72. Chowell G, Echevarria-Zuno S, Viboud C, Simonsen L, Tamerius J, Miller MA, et al. Characterizing the epidemiology of the 2009 influenza A/H1N1 pandemic in Mexico. *PLoS Med* 2011;8(5):e1000436.
73. Herrera-Valdez MA, Cruz-Aponte M, Castillo-Chavez C. Multiple outbreaks for the same pandemic: Local transportation and social distancing explain the different "Waves" of A-H1N1PDM cases observed in Mexico during 2009. *Mathematical Biosciences and Engineering* 2011;8(1):21-48.
74. Chowell G, Viboud C, Munayco CV, Gomez J, Simonsen L, Miller MA, et al. Spatial and temporal characteristics of the 2009 A/H1N1 influenza pandemic in Peru. *PLoS ONE* 2011;6(6):e21287.
75. Monto AS, Davenport FM, Napier JA, Francis Jr T. Modification of an outbreak of influenza in tecumseh, michigan by vaccination of schookhildren. *J.Infect.Dis* 1970;122(1-2):328-32.
76. Bootsma MC, Ferguson NM. The effect of public health measures on the 1918 influenza pandemic in U.S. cities. *Proc Natl Acad Sci U S A* 2007;104(18):7588-93.
77. Hatchett RJ, Mecher CE, Lipsitch M. Public health interventions and epidemic intensity during the 1918 influenza pandemic. *Proc Natl Acad Sci U S A* 2007;104(18):7582-7.
78. Markel H, Lipman HB, Navarro JA, Sloan A, Michalsen JR, Stern AM, et al. Nonpharmaceutical interventions implemented by US cities during the 1918-1919 influenza pandemic.[Erratum appears in JAMA. 2007 Nov 21;298(19):2264]. *Jama* 2007;298(6):644-54.
79. Jordan EO, Redd DB, Fink EB. Influenza in three Chicago groups. *Public Health Rep* 1919;34(28):1528-45.
80. Armstrong C, Hopkins R. An epidemiological study of the 1920 epidemic of influenza in an isolated rural community. *Public Health Reports* 1921;36(29):1671-702.
81. Winslow C-EA, Rogers JF. Statistics of the 1918 Epidemic of Influenza in Connecticut: With a consideration of the factors which influenced the prevalence of this disease in various communities *J Infect Dis* 1920;26(3):185-216.

# PRISMA 2009 Checklist

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 3 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | NA |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | NA |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 3-4 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 3-4 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | Appendix, p1 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 4 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 4 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 29 (Box 1) |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | NA |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 4 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | NA |

# PRISMA 2009 Checklist



| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | NA |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | NA |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 5, Figure 1 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | Appendix Tables 1 and 2 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | NA |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | NA |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | NA |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | NA |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | NA |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 12 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 12-16 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 16 |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 19 |

*From:* Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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# PRISMA 2009 Checklist

# School closures and influenza: systematic review of epidemiological studies


| | |
|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID: | bmjopen-2012-002149.R2 |
| Article Type: | Research |
| Date Submitted by the Author: | 23-Jan-2013 |
| Complete List of Authors: | Jackson, Charlotte; London School of Hygiene and Tropical Medicine,<br>Vynnycky, Emilia; Health Protection Agency,<br>Hawker, Jeremy; Health Protection Agency,<br>Olowokure, Babatunde; Health Protection Agency,<br>mangtani, punam; London School of Hygiene and Tropical Medicine, |
| <b>Primary Subject Heading</b>: | Epidemiology |
| Secondary Subject Heading: | Epidemiology, Infectious diseases, Public health |
| Keywords: | EPIDEMIOLOGY, Epidemiology < INFECTIOUS DISEASES, Public health < INFECTIOUS DISEASES, PUBLIC HEALTH, SYSTEMATIC REVIEWS |
| | |

# School closures and influenza: systematic review of epidemiological studies

Charlotte Jackson[1], Emilia Vynnycky[2], Jeremy Hawker[3], Babatunde Olowokure[3], Punam Mangtani[1]

[1] London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK; [2] Health Protection Agency, Colindale, London NW9 5EQ, UK; [3] Health Protection Agency, 5 St Philips Place, Birmingham B3 2PW, UK

Corresponding author: Charlotte Jackson, Room 113, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT.

Email: charlotte.jackson@lshtm.ac.uk

Tel: +44 (0) 207 927 2209

Word count: 3990

***Summary***

*Article focus*

- This systematic review assesses the effects of school closures on transmission of influenza, including data from the recent 2009 pandemic as well as from previous pandemics and seasonal outbreaks.

*Key messages*

- The available data suggest that school closure can be a useful intervention during influenza outbreaks, with the greatest benefits occurring amongst school-aged children.

*Strengths and limitations*

- We have reviewed an extensive body of literature on the effects of school closure on the incidence and transmission of influenza.
- The optimum timing and duration of closure are unclear because studies often differed in several respects, or used other interventions in addition to school closure.

*Abstract*

Objective: To review the effects of school closures on pandemic and seasonal influenza outbreaks.

Design: Systematic review.

Data sources: Medline and Embase, reference lists of identified articles, hand searches of key journals, and additional papers from the authors' collections.

Study selection: Studies were included if they reported on a seasonal or pandemic influenza outbreak coinciding with a planned or unplanned school closure.

Results: Of 2579 papers identified through Medline and Embase, 65 were eligible for inclusion in the review along with 14 identified from other sources. Influenza incidence frequently declined after school closure. The effect was sometimes reversed when schools reopened, supporting a causal role for school closure in reducing incidence. Any benefits associated with school closure appeared to be greatest amongst school-aged children. However, as schools often closed late in the outbreak or other interventions were used concurrently, it was sometimes unclear how much school closure contributed to the reductions in incidence.

Conclusions: School closures appear to have the potential to reduce influenza transmission, but the heterogeneity in the data available means that the optimum strategy (e.g. the ideal length and timing of closure) remains unclear.

***Introduction***

During the 2009 influenza pandemic, schools were closed in many settings in efforts to reduce transmission. The World Health Organization does not specifically recommend or discourage school closures during an influenza pandemic, as their potential benefits and harms may be context-specific [1], but has suggested that they be considered as part of a mitigation strategy [2]. Their effects on transmission, however, remain poorly understood [3,4]. Closures may be pro-active (occurring before transmission is established in the school) or reactive (a response to a school-based outbreak), and may involve closure of whole school(s) or dismissal of individual classes [4].

A review of the evidence available before the 2009 pandemic concluded that school closures may be beneficial, depending on characteristics including age-specific attack rates [4]. Here, we review epidemiological studies to assess the effects of school closures on transmission and incidence of seasonal and pandemic influenza, updating and extending previous reviews [2,4] to include data from the 2009 pandemic.

***Methods***

*Search strategy and selection criteria*

Medline and Embase were searched in January 2012, without language restrictions, for relevant papers published by the end of 2011 (see Appendix for search strategy). *Eurosurveillance* (23 April 2009 to 15 December 2011), *Morbidity and Mortality Weekly Report* (24 April 2009 to 23 December 2011) and *Emerging Infectious Diseases* (April 2009 to December 2011) were hand-searched. Results were supplemented using the reference lists of the articles identified, and papers from the reviewers' collections. An additional Pubmed search (for the words “influenza” and “school”) was used to identify relevant papers published during October – December 2011 but not yet listed in Medline or Embase.

Studies were included if they described one or more influenza outbreaks during which schools were initially open and subsequently closed, with or without other interventions. If papers presented several measures of influenza activity, the most specific data were extracted (e.g. data on laboratory-confirmed influenza were extracted in preference to all-cause school absenteeism). Studies using modelling techniques to assess how school closure affected transmission based on real epidemic curves were eligible; however, predictive modelling studies exploring how school closure might affect a hypothetical outbreak were excluded. English translations (where available) of the titles and abstracts of papers written in other languages were screened, but these papers were ineligible for inclusion. Studies of outbreaks which started during school closure were excluded.

Abstracts and full text were screened initially by one reviewer (CJ) and by a second reviewer (PM) if the first reviewer was in doubt as to the paper’s eligibility. Box 1 summarises the information extracted (by CJ) from the studies. Where possible, epidemic curves were plotted by transcribing daily or weekly data from figures or tables.

*Data analysis*

We summarised the data graphically and descriptively. We plotted the peak and cumulative attack rates (and 95% confidence intervals, calculated using standard methods for calculating CIs for proportions) for each study that provided an appropriate denominator. We calculated the normalised peak (peak AR / median AR) for datasets with a median AR greater than zero, to adjust approximately for differences in case definitions (this approach has been used elsewhere to adjust for intercity differences in case fatality proportions [5]). These estimates were stratified by the timing of closure, i.e. whether schools closed before, coincident with, or after the peak.

***Results***

Of 2579 papers identified through Medline and Embase, 430 were reviewed in full. 65 of these studies were included in the review, along with 14 additional papers (Figure 1; the supplementary PubMed search yielded no further eligible articles). 79 papers were thus included: 23 for seasonal and 56 for pandemic influenza (49, one, and seven from the 2009, 1968 and 1918 pandemics, respectively). Details of the studies are given in Table 1 and Supplementary Tables 1 and 2.

*Description of the epidemics*

19 and 41 epidemic curves were available on seasonal and pandemic influenza, respectively (Supplementary Figures 1 and 2). School closure was often followed by a reduction in incidence, in children specifically or the general population. However, closure often occurred late in the outbreaks (Table 1), and it is unclear whether it influenced the decline.

The cumulative and peak ARs varied widely for seasonal and pandemic influenza (Figure 2). Normalised peaks partly account for differences in case definitions between studies, but also varied considerably (Figure 3). There was no clear pattern in the cumulative, peak or normalised peak ARs plotted by timing of closure in relation to the peak. Relatively few schools closed before the peak (Figures 2 and 3); of those that did, two also reopened before the peak [6 7]. However, early introduction of non-pharmaceutical interventions (NPIs), often including school closures, in US cities during the 1918 pandemic has been found to be associated with reductions in mortality [5 8 9]. In Connecticut in 1918, three cities which closed schools experienced higher mortality rates than two which did not [10].

*Age-specific effects of school closure*

The available age-specific data suggested that any benefits associated with school closure were greatest amongst school-aged children [11-25]. In New Zealand during the 2009 pandemic, the age-standardised proportion of confirmed cases in 5-19 year-olds fell during the winter holiday and increased when schools reopened [19]; a slight increase in ILI consultation rates when schools reopened was confined to 5-14 year-olds [14]. Similar relationships between school closure and the ratio of the number of H1N1 infections in 5-20 year-olds to that in other age groups were reported for Mexico [23] and Peru [26]. During the 1967-68 influenza season in Great Britain, GP consultation rates for ILI amongst 5-14 year-olds declined during the Christmas holiday and increased when schools reopened; this effect was less clear in other age groups [17].

Winter holidays in Israel were associated with a reduction in the ratio between the number of clinic visits for influenza and those for non-respiratory complaints, in 6-12 year-olds, in three of five seasonal influenza periods studied [15]. In one season, this ratio was also reduced in adults, and in another it was reduced for adults not living with 6-12 year-olds. When a two-week teachers' strike coincided with an influenza outbreak in January 2000, closing 80% of elementary schools nationwide, this ratio decreased by 15% for 6-12 year-olds (95% CI 6-23%), but not for older individuals. As the authors note, children comprise a high proportion (34%) of the Israeli population, which may contribute to any apparent benefit of closing schools in Israel [27].

Similar data from four influenza seasons in Arizona are less consistent, partly because school closure rarely coincided with elevated influenza activity [18]. During all four seasons, rates of laboratory-confirmed influenza in school-aged children were similar during the two-week winter holiday and the preceding two weeks. In two seasons this rate increased in the two weeks after schools reopened; in one other season, it was significantly lower on reopening than during closure [18]. In comparison, rates in adults and pre-school-aged children increased successively (though not always significantly) across the three two-week periods in three of the seasons [18].

Three studies which fitted transmission models to surveillance data also concluded that school closures mainly benefit children [12 13]. Analyses of French seasonal ILI data [13] and ILI data from London during the 2009 pandemic [22] estimated that school holidays did not affect adults' contact patterns; similarly, reductions in transmission following school closures in Hong Kong in 2009 occurred primarily amongst children [12].

However, two studies of the 2009 pandemic suggested that school closure affected incidence in adults. One of these studies estimated the age-specific number of ILI cases due to pandemic H1N1 in England; estimated case numbers in most age groups decreased during the summer holiday and increased when schools reopened [25]. In Vojvodina, Serbia, incidence decreased amongst 5-14 and 15-64 year-olds during a one-week school closure [28].

*Reversibility of effects*

Incidence sometimes rebounded when schools reopened, suggesting that school closure contributed to reducing incidence in some settings. For example, during the 2009 pandemic in England, the estimated weekly number of infections declined during the school summer holiday; a second wave occurred when schools reopened (Supplementary Figure 2) [22 29]. Similar reversibility appeared in ILI consultation rates in Vojvodina in 2009 [28]. Datasets from the 2009 pandemic in Mexico [23 30 31] also suggested an increase in incidence after schools reopened (Supplementary Figure 2). Analyses of NPIs (usually including school closures) during the 1918 pandemic found that, in the cities studied, second waves occurred only after NPIs were lifted [5 8].

In the Israeli data regarding seasonal influenza and the teachers' strike, the number of physician visits for acute respiratory illness was 42% lower during closure compared to the previous two weeks; incidence increased after the strike [27]. During the 1999-2000 influenza season in Japan, the increase in incidence appeared to slow during the two-week winter holiday and accelerated when schools reopened [7]. Similarly, in Beijing in 2009, the cumulative incidence of laboratory-confirmed H1N1 influenza increased more markedly before and after a national school holiday than during the break [32].

*Changes in transmission patterns from modelling analyses of epidemic data*

Several studies have fitted transmission models to observed epidemic data to estimate the reduction in contact rates associated with school closure. School holidays were estimated to reduce transmission of seasonal influenza amongst children by a median of 24% (range 20-29%), based on rates of ILI in France from 1985 to 2006, corresponding to a 16-18% reduction in total case numbers [13]. During the 2009 pandemic in London, contact amongst 5-14 year-olds was reduced by an estimated 72% during the six-week summer holiday; the corresponding reduction during one-week half term holidays was 48% [22]. In US cities in 1918, changes in mortality were attributed to a combination of formal interventions (including school closure) and spontaneous social distancing [8]. In Sydney in 1918, formal and spontaneous social distancing together were estimated to have reduced contact rates by up to 38% [33]. Based on influenza incidence data from the 2009 pandemic in Mexico City, school closure together with other interventions appeared to reduce the population contact rate by 23% [31]. A subsequent analysis of national data from Mexico estimated that the contact rate was reduced by 30% during the intervention period [23].

In Hong Kong (also during the 2009 pandemic), closing primary schools, kindergartens, and childcare centres pro-actively, together with affected secondary schools, was estimated to reduce transmission by 70% amongst children and 25% in the population overall [12]. The same study estimated the effective reproduction number ($R_n$, the average number of secondary infectious persons generated by a single infectious person in a given population) as 1·7 before school closure, 1·5 during school closure, and 1·1 during the subsequent school holidays [12]. Daily estimates of $R_n$ in Hong Kong in 2009 (based on a longer time series) also suggested a decline during school closure and a slight increase following reopening [34].

Modelling techniques have also been used to estimate daily values of $R_n$ during a seasonal influenza outbreak in Hong Kong [35] and the 2009 pandemic in Mexico City [23 31] and New Zealand [19]. The Hong Kong analysis for seasonal influenza suggested that $R_n$ was not substantially affected by school closure, perhaps because closure occurred late in the outbreak when $R_n$ was already below one [35]. In Mexico City [31] and New Zealand, $R_n$ was declining before schools closed and continued to decrease during closure; in New Zealand, $R_n$ increased briefly but not substantially when schools reopened [19]. Analysis of a further outbreak in the USA detected no clear effect of school closure on transmission, which was attributed to the late timing of closure [20].

Modelling analyses of the spatiotemporal spread of pandemic H1N1 in Europe in 2009 were able to reproduce observed incidence patterns only when contact rates were allowed to change specifically during each country's school holidays (holidays were assumed to eliminate transmission in schools and increase community transmission by a factor of 1.4) [36]. In all countries, holidays were estimated to delay the peak compared to a hypothetical situation without school closure. In contrast, regression analysis of estimates of $R_n$ in 12 European countries found no evidence of an effect of school holidays on transmission in the nine countries in which school holidays coincided with the study period [37]. The authors proposed that this apparent lack of effect might result from changes in reporting, stochastic effects early in the outbreaks, and the fact that in some countries (including England), school holidays occurred outside the study period.

*Different school closure strategies*

In some outbreaks, individual schools were closed; in others, school closure was more widespread (Supplementary Tables 1 and 2). The effects of these different strategies could not be compared, due to both late implementation and differences between the studies in other factors (such as the duration of closure).

Analyses of the 1918 pandemic in US cities found that the duration of NPIs was negatively associated with the total excess death rate [9]. In the datasets reviewed here, closures longer than two weeks were associated with reduced incidence or transmission in several studies of seasonal [38] and pandemic [12 29] influenza, but not in others [11 39]. Two studies which suggested reasonably strong evidence of an effect of school closure (from France and Israel) reported on closures lasting two weeks [13 27]. Studies in Japan [7] and England and Wales [17] also suggested possible effects of two-week closures on seasonal influenza. However, two-week closures did not always appear to reduce transmission [35]. Shorter closures, e.g. of 1-2 weeks, may sometimes have contributed to reductions in transmission [22 29 31 32 40], but often had no obvious effect [41-44]. In London, contacts between children were reduced more dramatically during a six-week holiday than during one-week breaks, but this may reflect different behaviour during the different holidays [22].

*Use of multiple interventions*

In most of the pandemic influenza studies, other interventions were implemented alongside school closure and may have contributed to any reduction in incidence. In 2009, antiviral treatment and / or prophylaxis was commonly used in the studies identified [12 14 19 20 39 40 42 45-57]. Public places were sometimes closed and / or large gatherings were discouraged or restricted [16 30 31 58]. Some datasets from the 2009 pandemic included vaccination against the pandemic strain, although this was usually only available late in the study period so would not affect the included incidence data [29 32 57 59]. In 1918, school closures were often combined with other social distancing measures [5 8 9 33]; the only study included from the 1968 pandemic was a vaccine trial [60]. Of the few pandemic studies which mentioned no additional interventions, one suggested an effect of school closures: in Israel in 2009, three waves of infection corresponded to the planned closure and reopening of schools [61]. In the England and Wales data for the 2009 pandemic, other interventions (vaccination and antivirals) were used to only a limited extent; incidence still clearly declined during the school summer holiday and increased afterwards [29].

Some studies of seasonal influenza mentioned additional interventions (e.g. vaccination [62-64], prophylactic amantadine [65], hygiene promotion [38 41 66], closure of public places [38], and advice

to avoid large gatherings [44]). However, some studies without additional interventions showed reductions in incidence and / or transmission during school closure [13 27].

*Discussion*

This systematic review of the effects of school closures on influenza outbreaks extends previous reviews [2 4] to include published experiences from the 2009 pandemic. The results suggest that school closure can reduce transmission of pandemic [12] and seasonal [13 27] influenza amongst schoolchildren. Many datasets, however, show no clear effect of school closure. As noted by some authors [20 43 44], this may sometimes have been because schools shut late in the outbreak (often close to or after the peak).

In some studies, incidence increased when schools reopened [5 7 8 14 22 27 29 31]. This apparent reversibility provides evidence that school closure can cause reductions in influenza incidence. In two of the studies of seasonal influenza which showed reversibility [7 27], no additional interventions (beyond usual seasonal interventions) were used. In many other datasets, multiple interventions were used, so the specific effects of school closures are difficult to isolate.

In 2009, several countries closed schools whilst in others, planned holidays coincided with outbreaks. Several datasets from this pandemic strengthen support for school closure as an intervention; however, others illustrate that benefits are not guaranteed and that timely closure may be challenging. The sensitivity of the 2009 pandemic to school closures probably reflects the high attack rates in children compared to adults; outbreaks in which children are less affected might be less sensitive to school closure.

Studies presenting age-stratified data suggested that the effects of school closure on transmission were greater amongst children than adults. Few studies stratified children further, e.g. into primary and secondary school students. Older children might socialise more than younger children during school closures, so closing primary schools may have a greater effect on transmission than closing secondary schools (e.g. in Hong Kong in 2009, primary schools were closed pro-actively whilst secondary schools closed if cases occurred amongst their students [12]).

The long term effects of closing schools are unclear, as relatively few studies presented substantial data after schools reopened. For example, school closure could result in multiple peaks, potentially involving more cases than would otherwise have occurred [8]. However, a study published since this review was conducted estimated that case numbers in Alberta, Canada, could have been up to twice as high as those seen if schools had not closed for planned holidays [67]. It is difficult to compare reactive versus pro-active closures, different durations of closure, and local versus national closures as studies typically differed in several respects.

Some studies have concluded that reopening schools after holiday periods can accelerate epidemic growth (e.g. during the 1957 [68 69] and 2009 [70] pandemics). These studies were beyond the scope of this review of the effects of closing schools during outbreaks, but they suggest that extending school holidays might delay the spread of an epidemic beginning during a break.

Results from analyses of seasonal influenza may not be directly applicable to a pandemic. Schools were often closed for planned holidays rather than in response to the outbreaks; contact patterns may differ between reactive school closures [71] and holidays [72]. Extrapolating from previous pandemics may also be problematic. Modelling studies [73-75] have predicted that school closures will have the greatest effects if transmission occurs mainly amongst children. The importance of children in transmission has varied between pandemics [76]; in 2009, attack rates were higher in children than in adults, probably because of pre-existing immunity in older individuals [77]. Viral virulence will also influence individuals' responses to school closure and other interventions, e.g. spontaneous social distancing during a mild pandemic may be less dramatic than occurred in 1918. Changes in household size, contact patterns, children's behaviour and school systems since 1918, 1957 and 1968 may also limit the generalisability of experiences from these pandemics. As noted in a study of the 1918 pandemic in Connecticut, reverse causality may occur when comparing rates in cities which closed schools to those in cities which did not, if closure was a response to a particularly severe local outbreak [10].

One limitation of the datasets is that ascertainment may have changed during the outbreaks, due to changes in surveillance and care-seeking behaviour. Increases in ascertainment during an outbreak could obscure any reductions in incidence during school closures (e.g. in one study, enhanced surveillance began the day the school closed [56]). Conversely, the proportion of patients who undergo virological testing may be reduced late in an outbreak, and in some settings (e.g. New Zealand [14]) patients with ILI were discouraged from consulting GPs during the 2009 pandemic. The estimated proportion of influenza cases that were reported in Hong Kong declined to ~5% of its original value during the move from containment to mitigation during the 2009 pandemic [12]. In England, the introduction of the National Pandemic Flu

Service telephone helpline coincided with the school holiday, and was estimated to have reduced the probability of GP consultation for adults with ILI from 16% to 1.8% [22].

Case definitions may not always have been well-suited to detecting any effect of school closure. For example, school absenteeism is a relatively non-specific measure, whilst laboratory specimens frequently represent severe infections (e.g. in the elderly, who may have little contact with children and therefore be relatively unaffected by school closure).

Influenza transmission is influenced by factors besides contact in schools, including temperature and absolute humidity (AH) [78-81]. Two studies which assessed the role of AH during the 2009 pandemic did not find strong evidence that it affected transmission [24 37]. The two waves seen in the UK in 2009 could be explained by changes in contact patterns during school holidays [29 82]. In a modelling study of data from Alberta, Canada, the best-fitting model included effects of temperature and school holidays on transmission, and predicted that if schools had not closed, the outbreak would have been restricted by temperature effects but would still have been 2.1 times larger than was observed in the province as a whole (1.38 and 1.54 times in the cities of Calgary and Edmonton, respectively) [67]. A study of the interplay between school calendars, AH and population susceptibility in enhancing influenza transmission concluded that high AH may prevent influenza outbreaks [79]. However, if a sufficiently high proportion of the population is susceptible, outbreaks can occur even when AH is high; the opening of schools may enhance transmission [79]. Taken together, these studies suggest that contact in schools is not the only determinant of influenza transmission, but it is one influential (and modifiable) factor.

Previous studies have estimated the effects of public health interventions using transmission models [8 12 20 31]. The development of such models is complicated for the datasets reviewed here, and would not necessarily have provided conclusive insight into the impact of school closures. For example, many factors are unknown and would need to be estimated or assumed for each dataset, such as the basic reproduction number, proportion of infections that were reported, the effect of other interventions, and the proportion of individuals who were immune at the start of the outbreak.

The review was limited to published studies, which could potentially introduce publication bias. However, many of the studies identified did not aim to evaluate the effects of school closure on transmission, so publication bias appears unlikely. This is supported by the apparent lack of an effect of school closure in many of the studies (including some of those which did specifically assess school closure as an intervention). A further limitation is that most papers were screened (and all data were extracted) by a single reviewer. Foreign language papers were excluded, but in most cases it was clear from the title and / or abstract (available in English) that the papers were not relevant to this review.

***Conclusions***

The available data suggest that school closures can potentially reduce transmission during an influenza outbreak, even in the absence of other interventions, although the optimal school closure strategy is unclear. The effect of school closures is larger for school-aged children than for other age groups, although there is some evidence that incidence in adults might also be reduced. During a future pandemic (or seasonal outbreaks during which schools are closed), it will be important to collect incidence data using systematic ascertainment and a consistent case definition, before, during and after school closure, to assess the effects of school closures on transmission. Analysis of comparable data from multiple outbreaks may help to overcome some of the problems with comparability and ascertainment discussed above, and clarify which features determine the effectiveness of school closures. Although timely school closures may reduce transmission, other implications of school closure (e.g. ethical and economic considerations) [4], and viral properties such as virulence, must also be considered in policy decisions, and may depend on the local context [1].

*Acknowledgements*

This paper developed from a review commissioned by the UK Health Protection Agency as part of its pandemic influenza programme. We thank Nadia Inglis, Angus Nicoll and two anonymous members of the HPA's Influenza and Respiratory Virus Programme Board for helpful comments on the review. We also thank staff at the LSHTM library for assistance in locating papers.

*Funding*

This work was partially funded by the Health Protection Agency; C.J. was supported by a Research Training Fellowship from the National Institute for Health Research.

*Role of the funding source*

NIHR had no role in the design and conduct of the study; collection, analysis or interpretation of data; writing of the report; or the decision to submit the article for publication. The HPA commissioned the research.

*Access to data*

All authors had full access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

*Data sharing*

No additional data available.

*Competing interest statement*

All authors have completed the Unified Competing Interest form at http://www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: funding from NIHR and HPA; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

*Statement of authors' roles*

B.O and J.H. had the initial idea. P.M., C.J. and E.V. developed the research questions and study design. C.J. carried out the literature review and P.M. assessed any doubtful papers. C.J., P.M. and E.V. analysed data. C.J., P.M. and E.V. wrote the paper. J.H. commented on outputs and contributed to the final draft. J.H. and B.O. contributed to the final draft.

*Ethical approval*

Not required.

***References***

1. World Health Organization. Reducing transmission of pandemic (H1N1) 2009 in school settings. A framework for national and local planning and response, 2009.
2. Bell DM, World Health Organization Writing Group. Non-pharmaceutical interventions for pandemic influenza, national and community measures. *Emerg Infect Dis* 2006;12(1):88-94.
3. Aledort JE, Lurie N, Wasserman J, et al. Non-pharmaceutical public health interventions for pandemic influenza: an evaluation of the evidence base. *BMC Public Health* 2007;7:208.
4. Cauchemez S, Ferguson NM, Wachtel C, et al. Closure of schools during an influenza pandemic. *The Lancet Infectious Diseases* 2009;9(8):473-81.
5. Hatchett RJ, Mecher CE, Lipsitch M. Public health interventions and epidemic intensity during the 1918 influenza pandemic. *Proc Natl Acad Sci U S A* 2007;104(18):7582-7.
6. Olson JG. School absenteeism during an outbread of B/Hong Kong/5/72-like influenze virus in Taipei, Taiwan. *Southeast Asian J Trop Med Public Health* 1980;11(4):429-34.
7. Fujii H, Takahashi H, Ohyama T, et al. Evaluation of the school health surveillance system for influenza, Tokyo, 1999-2000. *Japanese Journal of Infectious Diseases* 2002;55(3):97-98.
8. Bootsma MC, Ferguson NM. The effect of public health measures on the 1918 influenza pandemic in U.S. cities. *Proc Natl Acad Sci U S A* 2007;104(18):7588-93.
9. Markel H, Lipman HB, Navarro JA, et al. Nonpharmaceutical interventions implemented by US cities during the 1918-1919 influenza pandemic.[Erratum appears in JAMA. 2007 Nov 21;298(19):2264]. *Jama* 2007;298(6):644-54.
10. Winslow C-EA, Rogers JF. Statistics of the 1918 Epidemic of Influenza in Connecticut: With a consideration of the factors which influenced the prevalence of this disease in various communities *J Infect Dis* 1920;26(3):185-216.
11. Armstrong C, Hopkins R. An epidemiological study of the 1920 epidemic of influenza in an isolated rural community. *Public Health Reports* 1921;36(29):1671-702.
12. Wu JT, Cowling BJ, Lau EH, et al. School closure and mitigation of pandemic (H1N1) 2009, Hong Kong. *Emerg Infect Dis* 2010;16(3):538-41.
13. Cauchemez S, Valleron A-J, Boelle P-Y, Flahault A, Ferguson NM. Estimating the impact of school closure on influenza transmission from Sentinel data. *Nature* 2008;452(7188):750-4.
14. Baker MG, Wilson N, Huang QS, et al. Pandemic influenza A(H1N1)v in New Zealand: the experience from April to August 2009. *Euro Surveill* 2009;14(34).
15. Heymann AD, Hoch I, Valinsky L, et al. School closure may be effective in reducing transmission of respiratory viruses in the community. *Epidemiol Infect* 2009;137(10):1369-76.
16. Tinoco Y, Razuri H, Ortiz EJ, et al. Preliminary population-based epidemiological and clinical data on 2009 pandemic H1N1 influenza A (pH1N1) from Lima, Peru. *Influenza Other Respi Viruses* 2009;3(6):253-6.
17. Miller DL, Lee JA. Influenza in Britain 1967-68. *Journal of Hygiene* 1969;67:559-72.
18. Wheeler CC, Erhart LM, Jehn ML. Effect of school closure on the incidence of influenza among school-age children in Arizona. *Public Health Rep* 2010;125(6):851-9.
19. Paine S, Mercer GN, Kelly PM, et al. Transmissibility of 2009 pandemic influenza A(H1N1) in New Zealand: effective reproduction number and influence of age, ethnicity and importations. *Euro Surveill* 2010;15(24).

20. Cauchemez S, Bhattarai A, Marchbanks TL, et al. Role of social networks in shaping disease transmission during a community outbreak of 2009 H1N1 pandemic influenza. *Proc Natl Acad Sci U S A* 2011;108(7):2825-30.
21. Marchbanks TL, Bhattarai A, Fagan RP, et al. An outbreak of 2009 pandemic influenza A (H1N1) virus infection in an elementary school in Pennsylvania. *Clin Infect Dis* 2011;52 Suppl 1:S154-60.
22. Birrell PJ, Ketsetzis G, Gay NJ, et al. Bayesian modeling to unmask and predict influenza A/H1N1pdm dynamics in London. *Proceedings of the National Academy of Sciences of the United States of America* 2011;108(45):18238-43.
23. Chowell G, Echevarria-Zuno S, Viboud C, et al. Characterizing the epidemiology of the 2009 influenza A/H1N1 pandemic in Mexico. *PLoS Med* 2011;8(5):e1000436.
24. Chowell G, Viboud C, Munayco CV, et al. Spatial and temporal characteristics of the 2009 A/H1N1 influenza pandemic in Peru. *PLoS ONE* 2011;6(6):e21287.
25. Evans B, Charlett A, Powers C, et al. Has estimation of numbers of cases of pandemic influenza H1N1 in England in 2009 provided a useful measure of the occurrence of disease? *Influenza and other Respiratory Viruses* 2011;5(6):e504-e12.
26. Munayco CV, Gomez J, Laguna-Torres VA, et al. Epidemiological and transmissibility analysis of influenza A(H1N1)v in a southern hemisphere setting: Peru. *Euro surveillance : bulletin europeen sur les maladies transmissibles = European communicable disease bulletin* 2009;14(32).
27. Heymann A, Chodick G, Reichman B, et al. Influence of school closure on the incidence of viral respiratory diseases among children and on health care utilization. *Pediatr Infect Dis J* 2004;23(7):675-7.
28. Petrovic V, Seguljev Z, Cosic G, et al. Overview of the winter wave of 2009 pandemic influenza A(H1N1)v in Vojvodina, Serbia. *Croatian Medical Journal* 2011;52(2):141-50.
29. Baguelin M, Hoek AJV, Jit M, et al. Vaccination against pandemic influenza A/H1N1v in England: A real-time economic evaluation. *Vaccine* 2010;28(12):2370-84.
30. Echevarria-Zuno S, Mejia-Arangure JM, Mar-Obeso AJ, et al. Infection and death from influenza A H1N1 virus in Mexico: a retrospective analysis. *Lancet* 2009.
31. Cruz-Pacheco G, Duran L, Esteva L, et al. Modelling of the influenza A(H1N1)v outbreak in Mexico City, April-May 2009, with control sanitary measures. *Euro Surveill* 2009;14(26).
32. Wu J, Xu F, Lu L, et al. Safety and effectiveness of a 2009 H1N1 vaccine in Beijing. *New England Journal of Medicine* 2010;363(25):2416-23.
33. Caley P, Philp DJ, McCracken K. Quantifying social distancing arising from pandemic influenza. *Journal of the Royal Society Interface* 2008;5(23):631-9.
34. Cowling BJ, Lau MSY, Ho LM, et al. The effective reproduction number of pandemic influenza: Prospective estimation. *Epidemiology* 2010;21(6):842-46.
35. Cowling BJ, Lau EHY, Lam CLH, et al. Effects of school closures, 2008 winter influenza season, Hong Kong. *Emerg Infect Dis* 2008;14(10):1660-2.
36. Merler S, Ajelli M, Pugliese A, et al. Determinants of the spatiotemporal dynamics of the 2009 H1N1 pandemic in europe: Implications for real-time modelling. *PLoS Computational Biology* 2011;7(9).
37. Flasche S, Hens N, Boëlle P-Y, et al. Different transmission patterns in the early stages of the influenza A(H1N1)v pandemic: A comparative analysis of 12 European countries. *Epidemics* 2011;3(2):125-33.
38. Lo JY, Tsang TH, Leung YH, et al. Respiratory infections during SARS outbreak, Hong Kong, 2003. *Emerg Infect Dis* 2005;11(11):1738-41.

39. Gomez J, Munayco C, Arrasco J, et al. Pandemic influenza in a southern hemisphere setting: the experience in Peru from May to September, 2009. *Euro Surveillance: Bulletin Europeen sur les Maladies Transmissibles = European Communicable Disease Bulletin* 2009;14(42).
40. Kawaguchi R, Miyazono M, Noda T, et al. Influenza (H1N1) 2009 outbreak and school closure, Osaka Prefecture, Japan. *Emerg Infect Dis* 2009;15(10):1685.
41. Danis K, Fitzgerald M, Connell J, et al. Lessons from a pre-season influenza outbreak in a day school. *Commun Dis Public Health* 2004;7(3):179-83.
42. Calatayud L, Kurkela S, Neave PE, et al. Pandemic (H1N1) 2009 virus outbreak in a school in London, April-May 2009: an observational study. *Epidemiol Infect* 2010;138(2):183-91.
43. Rodriguez CV, Rietberg K, Baer A, et al. Association between school closure and subsequent absenteeism during a seasonal influenza epidemic. *Epidemiology* 2009;20(6):787-92.
44. Johnson AJ, Moore ZS, Edelson PJ, et al. Household responses to school closure resulting from outbreak of influenza B, North Carolina. *Emerg Infect Dis* 2008;14(7):1024-30.
45. Smith A, Coles S, Johnson S, et al. An outbreak of influenza A(H1N1)v in a boarding school in South East England, May-June 2009. *Euro Surveill* 2009;14(27):9.
46. Effler PV, Carcione D, Giele C, et al. Household responses to pandemic (H1N1) 2009-related school closures, Perth, Western Australia. *Emerg Infect Dis* 2010;16(2):205-11.
47. Health Protection Agency West Midlands H1N1v Investigation Team. Preliminary descriptive epidemiology of a large school outbreak of influenza A(H1N1)v in the West Midlands, United Kingdom, May 2009. *Euro Surveill* 2009;14(27).
48. Wallensten A, Oliver I, Lewis D, et al. Compliance and side effects of prophylactic oseltamivir treatment in a school in South West England. *Euro Surveill* 2009;14(30):19285.
49. Strong M, Burrows J, Stedman E, et al. Adverse drug effects following oseltamivir mass treatment and prophylaxis in a school outbreak of 2009 pandemic influenza A(H1N1) in June 2009, Sheffield, United Kingdom. *Euro Surveill* 2010;15(19):pii/19565.
50. Guinard A, Grout L, Durand C, et al. Outbreak of influenza A(H1N1)v without travel history in a school in the Toulouse district, France, June 2009. *Euro Surveill* 2009;14(27).
51. France AM, Jackson M, Schrag S, et al. Household transmission of 2009 influenza A (H1N1) virus after a school-based outbreak in New York City, April-May 2009. *J Infect Dis* 2010;201(7):984-92.
52. Lessler J, Reich NG, Cummings DAT, New York City Department of H, Mental Hygiene Swine Influenza Investigation T, Nair HP, et al. Outbreak of 2009 pandemic influenza A (H1N1) at a New York City school. *N Engl J Med* 2009;361(27):2628-36.
53. Nishiura H, Castillo-Chavez C, Safan M, et al. Transmission potential of the new influenza A(H1N1) virus and its age-specificity in Japan. *Euro Surveill* 2009;14(22):4.
54. Shimada T, Gu Y, Kamiya H, et al. Epidemiology of influenza A(H1N1)v virus infection in Japan, May-June 2009. *Euro Surveill* 2009;14(24).
55. Carrillo-Santisteve P, Renard-Dubois S, Cheron G, et al. 2009 pandemic influenza A(H1N1) outbreak in a complex of schools in Paris, France, June 2009. *Euro Surveill* 2010;15(25):24.
56. Huai Y, Lin J, Varma JK, et al. A primary school outbreak of pandemic 2009 influenza A (H1N1) in China. *Influenza other respi* 2010;4(5):259-66.

57. Poggensee G, Gilsdorf A, Buda S, et al. The first wave of pandemic influenza (H1N1) 2009 in Germany: From initiation to acceleration. *BMC Infectious Diseases* 2010;10(155).
58. Miller JC, Danon L, O'Hagan JJ, et al. Student behavior during a school closure caused by pandemic influenza A/H1N1. *PLoS ONE* 2010;5(5):e10425.
59. Hsueh P-R, Lee P-I, Hsiang Chiu A-W, et al. Pandemic (H1N1) 2009 vaccination and class suspensions after outbreaks, Taipei City, Taiwan. *Emerg Infect Dis* 2010;16(8):1309-11.
60. Monto AS, Davenport FM, Napier JA, et al. Modification of an outbreak of influenza in tecumseh, michigan by vaccination of schookhildren. *J.Infect.Dis* 1970;122(1-2):328-32.
61. Engelhard D, Bromberg M, Averbuch D, et al. Increased extent of and risk factors for pandemic (H1N1) 2009 and seasonal infl uenza among children, Israel. *Emerging Infectious Diseases* 2011;17(9):1740-43.
62. Briscoe JH. The protective effect of influenza vaccine in a mixed influenza A and B epidemic in a boys' boarding school. *J R Coll Gen Pract* 1977;27(166):28-31.
63. Farley TA, St. Germain JM, Chamberlain LA, et al. The impact of influenza vaccination on respiratory illness at a boarding School. *Journal of American College Health* 1992;41(3):127-31.
64. Sonoguchi T, Naito H, Hara M. Cross-subtype protection in humans during sequential, overlapping, and/or concurrent epidemics caused by H3N2 and H1N1 influenza viruses. *Journal of Infectious Diseases* 1985;151(1):81-88.
65. Davies JR, Grilli EA, Smith AJ, et al. Prophylactic use of amantadine in a boarding school outbreak of influenza A. *J R Coll Gen Pract* 1988;38(313):346-8.
66. Cashman P, Massey P, Durrheim D, et al. Pneumonia cluster in a boarding school--implications for influenza control. *Commun Dis Intell* 2007;31(3):296-8.
67. Earn DJ, He D, Loeb MB, et al. Effects of school closure on incidence of pandemic influenza in Alberta, Canada. *Ann Intern Med* 2012;156(3):173-81.
68. Brunyate WDT, Fleming GM, Llopis A, et al. The early stages of the 1957 influenza epidemic in England and Wales in relation to the re-assembly of schools. *Mon Bull Minist Hlth Lab Serv* 1961;20(MAY):88-92.
69. Dunn FL, Carey DE, Cohen A, et al. Epdemiologic studies of asian influenza in a louisiana parish. *Amer* 1959;J.Hyg. 70(3):351-71.
70. Chao DL, Halloran ME, Longini IM, Jr. School opening dates predict pandemic influenza A(H1N1) outbreaks in the United States. *J Infect Dis* 2010;202(6):877-80.
71. Jackson C, Mangtani P, Vynnycky E, et al. School Closures and Student Contact Patterns. *Emerg Infect Dis* 2011;17(2):245-47.
72. Eames KTD, Tilston NL, White PJ, et al. The impact of illness and the impact of school closure on social contact patterns. *Health Technol Assess* 2010;14(34):267-312.
73. Glass K, Barnes B. How much would closing schools reduce transmission during an influenza pandemic? *Epidemiology* 2007;18(5):623-8.
74. Vynnycky E, Edmunds WJ. Analyses of the 1957 (Asian) influenza pandemic in the United Kingdom and the impact of school closures. *Epidemiol Infect* 2008;136(2):166-79.
75. Milne GJ, Kelso JK, Kelly HA, et al. A small community model for the transmission of infectious diseases: comparison of school closure as an intervention in individual-based models of an influenza pandemic. *PLoS ONE* 2008;3(12):e4005.
76. Davis LE, Caldwell GG, Lynch RE. Hong Kong influenza: The epidemiologic features of a high school family study analyzed and compared with a similar study during the 1957Asian influenza epidemic. *American Journal of Epidemiology* 1970;92(4):520.

77. Miller E, Hoschler K, Hardelid P, et al. Incidence of 2009 pandemic influenza A H1N1 infection in England: a cross-sectional serological study. *Lancet* 2010;375(9720):1100-8.
78. Lowen AC, Mubareka S, Steel J, et al. Influenza Virus Transmission Is Dependent on Relative Humidity and Temperature. *PLoS Pathog* 2007;3(10):e151.
79. Shaman J, Goldstein E, Lipsitch M. Absolute humidity and pandemic versus epidemic influenza. *Am J Epidemiol* 2011;173(2):127-35.
80. Shaman J, Kohn M. Absolute humidity modulates influenza survival, transmission, and seasonality. *Proc Natl Acad Sci U S A* 2009;106(9):3243-8.
81. Shaman J, Pitzer VE, Viboud C, et al. Absolute humidity and the seasonal onset of influenza in the continental United States. *PLoS Biol* 2010;8(2):e1000316.
82. Eames KT, Tilston NL, Brooks-Pollock E, et al. Measured Dynamic Social Contact Patterns Explain the Spread of H1N1v Influenza. *PLoS Comput Biol* 2012;8(3):e1002425.
83. Uchida M, Tsukahara T, Kaneko M, et al. Swine-origin influenza a outbreak 2009 at Shinshu University, Japan. *BMC Public Health* 2011;11:79.

**Table 1:** Features of the studies identified. Studies may present more than one dataset and so appear in more than one row of each section.

| | | Number of studies |
|---|---|---|
| | ***Total studies*** | ***79*** |
| Type of outbreak | Seasonal | 22 |
| | 1918 pandemic | 7 |
| | 1968 pandemic | 1 |
| | 2009 pandemic | 49 |
| Setting | Europe | 22 |
| | North America | 22 |
| | Central America | 5 |
| | South America | 3 |
| | Asia | 20 |
| | Africa | 1 |
| | Australasia | 6 |
| Data provided on[1]: | Children only | 25 |
| | General population | 29 |
| | School pupils and staff | 5 |
| | Children and other specified groups separately | 22 |
| Reason for closure | High student absenteeism | 3 |
| | High staff absenteeism | 1 |
| | High student and staff absenteeism | 1 |
| | Other reactive closure[2] | 31 |
| | Pro-active | 7 |
| | Planned holiday | 38 |
| | Other[3] | 3 |
| | Unclear | 3 |
| Period of closure | Continuous | 67 |
| | Intermittent | 8 |
| | Variable[4] | 3 |
| | Not stated | 1 |
| Other interventions in place[5] | None | 20 |
| | Antivirals | 33 |
| | Other social distancing | 24 |
| | Vaccination | 8 |
| | Other | 20 |
| Timing of closure | Before peak | 21 |
| | Same day / week as peak | 9 |
| | After peak | 36 |
| | Variable[4] | 8 |
| | Unclear | 8 |
| Duration of closure[6] | <7 days | 8 |
| | 7-13 days | 33 |
| | 14-20 days | 19 |
| | ≥21 days | 17 |
| | Variable[4] | 6 |
| | Not stated | 2 |

[1] Each study may present more than one data source

[2] Closure in response to outbreak, not stated as being for operational reasons

[3] Teachers' strike (2 studies) or response to SARS outbreak (1 study)

[4] Studies of multiple US cities during the 1918 pandemic or multiple countries in 2009

[5] Described in the included paper or related papers; excludes normal levels of vaccine and antiviral usage in seasonal datasets.

[6] Each study may present more than one dataset for which the durations of closure differed

***Figure legends***

**Figure 1:** Identification of epidemiological studies of the effects of school closure on influenza outbreaks

**Figure 2:** Peak cumulative attack rates recorded in the identified studies. Case definitions varied between studies (see Appendix); only studies which included a denominator are shown. Studies which reported peak prevalence of absenteeism are denoted by an asterisk. See Appendix for full details of datasets. Abbreviations: BC, British Colombia; IL, Illinois; CT, Connecticut; NC, North Carolina; UK, United Kingdom; KI, Kelleys Island. All pandemic data are from 2009 except for Kelleys Island.

**Figure 3:** Normalised peak attack rates (estimated as peak attack rate / median attack rate) recorded in the identified studies; one study with an estimate normalised peak of 128 is excluded for clarity [83]. Case definitions varied between studies (see Appendix). Studies which reported peak prevalence of absenteeism are denoted by an asterisk. Abbreviations: HK, Hong Kong; IL, Illinois; SARI, severe acute respiratory infection; NC, North Carolina; UK, United Kingdom; KI, Kelleys Island.

**Box 1: Information extracted from eligible studies (where presented)**

Study design

Study population / setting (including size of population)

Nature of school closure (e.g. school holiday, response to outbreak)

Duration of closure and number of schools affected

Timing of closure in relation to influenza circulation

Outcome measure(s) examined (e.g. clinical ILI, virologically confirmed influenza)

Association between school closure and outcome

Epidemic curve (transcribed from graphs or figures); used to derive peak, cumulative and median attack rates

Normalised peak attack rate (= peak attack rate / median attack rate)

School closures and influenza: systematic review of epidemiological studies

Charlotte Jackson[1], Emilia Vynnycky[2], Jeremy Hawker[3], Babatunde Olowokure[3], Punam Mangtani[1]

[1] London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK; [2] Health Protection Agency, Colindale, London NW9 5EQ, UK; [3] Health Protection Agency, 5 St Philips Place, Birmingham B3 2PW, UK

Corresponding author: Charlotte Jackson, Room 113, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT.

Email: charlotte.jackson@lshtm.ac.uk

Tel: +44 (0) 207 927 2209

Word count: ~~399~~3990~~9~~

*Abstract*

Objective: To review the effects of school closures on pandemic and seasonal influenza outbreaks.

Design: Systematic review.

Data sources: Medline and Embase, reference lists of identified articles, hand searches of key journals, and additional papers from the authors' collections.

Study selection: Studies were included if they reported on a seasonal or pandemic influenza outbreak coinciding with a planned or unplanned school closure.

Results: Of 2579 papers identified through Medline and Embase, 65 were eligible for inclusion in the review along with 14 identified from other sources. Influenza incidence frequently declined after school closure. The effect was sometimes reversed when schools reopened, supporting a causal role for school closure in reducing incidence. Any benefits associated with school closure appeared to be greatest amongst school-aged children. However, as schools often closed late in the outbreak or other interventions were used concurrently, it was sometimes unclear how much school closure contributed to the reductions in incidence.

Conclusions: School closures appear to have the potential to reduce influenza transmission, but the heterogeneity in the data available means that the optimum strategy (e.g. the ideal length and timing of closure) remains unclear.

### *Introduction*

During the 2009 influenza pandemic, schools were closed in many settings in efforts to reduce transmission. The World Health Organization does not specifically recommend or discourage school closures during an influenza pandemic, as their potential benefits and harms may be context-specific [1], but has suggested that they be considered as part of a mitigation strategy [2]. Their effects on transmission, however, remain poorly understood [3 4]. Closures may be pro-active (occurring before transmission is established in the school) or reactive (a response to a school-based outbreak), and may involve closure of whole school(s) or dismissal of individual classes [4].

A review of the evidence available before the 2009 pandemic concluded that school closures may be beneficial, depending on characteristics ~~such as~~including age-specific attack rates [4]. Here, we review epidemiological studies to assess the effects of school closures on transmission and incidence of seasonal and pandemic influenza, updating and extending previous reviews [2 4] to include data from the 2009 pandemic.

### *Methods*

*Search strategy and selection criteria*

Medline and Embase were searched in January 2012, without language restrictions, for relevant papers published by the end of 2011 (see Appendix for search strategy). *Eurosurveillance* (23 April 2009 to 15 December 2011), *Morbidity and Mortality Weekly Report* (24 April 2009 to 23 December 2011) and *Emerging Infectious Diseases* (April 2009 to December 2011) were hand-searched. Results were supplemented ~~with papers from~~using the reference lists of the articles identified, and papers from the reviewers' collections. An additional Pubmed search (for the words "influenza" and "school") was used to identify relevant papers published during October – December 2011 but not yet listed in Medline or Embase.

Studies were included if they described one or more influenza outbreaks during which schools were initially open and subsequently closed, with or without other interventions. If papers presented several measures of influenza activity, the most specific data were extracted (e.g. data on laboratory-confirmed influenza were extracted in preference to all-cause school absenteeism). Studies ~~which used~~using modelling techniques to assess how school closure affected transmission based on real epidemic curves were eligible; however, predictive modelling studies exploring how school closure might affect a hypothetical outbreak were excluded. English translations (where available) of the titles and abstracts of papers written in other languages were screened, but these papers were ~~not~~ ineligible for inclusion. Studies of outbreaks which started during school closure were excluded.

Abstracts and full text were screened initially by one reviewer (CJ) and by a second reviewer (PM) if the first reviewer was in doubt as to the paper's eligibility~~necessary~~. Box 1 summarises the information extracted (by CJ) from the studies. Where possible, epidemic curves were plotted by transcribing daily or weekly data from figures or tables.

*Data analysis*

We summarised the data graphically and descriptively. We plotted the peak and cumulative attack rates (and 95% confidence intervals, calculated using standard methods for calculating CIs for proportions) for each study that provided an appropriate denominator. We calculated the normalised peak (peak AR / median AR) for datasets with a median AR greater than zero, to adjust approximately for differences in case definitions (this approach has been used elsewhere to adjust for intercity differences in case fatality proportions [5]). These estimates were stratified by the timing of closure, i.e. whether schools closed before, coincident with, or after the peak.

***Results***

Of 2579 papers identified through Medline and Embase, 430 were reviewed in full. 65 of these studies were included in the review, along with 14 additional papers (Figure 1; the supplementary PubMed search yielded no further eligible articles). 79 papers were thus included ~~in the review~~: 23 for seasonal and 56 for pandemic influenza (49, one, and seven from the 2009, 1968 and 1918 pandemics, respectively). Details of the studies are given in Table 1 and Supplementary Tables 1 and 2.

*Description of the epidemics*

19 and 41 epidemic curves were available on seasonal and pandemic influenza, respectively (Supplementary Figures 1 and 2). School closure was often followed by a reduction in incidence, in children specifically or the general population. However, closure often occurred late in the outbreaks (Table 1), and it is unclear whether it influenced the decline.

The cumulative and peak ARs varied widely for seasonal and pandemic influenza (Figure 2). Normalised peaks partly account for differences in case definitions between studies, but also varied considerably (Figure 3). There was no clear pattern in the cumulative, peak or normalised peak ARs plotted by timing of closure in relation to the peak. Relatively few schools closed before the peak (Figures 2 and 3); of those that did, two also reopened before the peak [6 7]. However, early introduction of non-pharmaceutical interventions (NPIs), ~~which~~

often includinged school closures, in US cities during the 1918 pandemic has been found to be associated with ~~a~~ reductions in mortality [5 8 9]. In Connecticut in 1918, three cities which closed schools experienced higher mortality rates than two which did not [10].

*Age-specific effects of school closure*

The available age-specific data suggested that any benefits associated with school closure were greatest amongst school-aged children [11-25]. In New Zealand during the 2009 pandemic, the age-standardised proportion of confirmed cases in 5-19 year-olds fell during the winter holiday and increased when schools reopened [19]; a slight increase in ILI consultation rates when schools reopened was confined to 5-14 year-olds [14]. Similar relationships between school closure and the ratio of the number of H1N1 infections in 5-20 year-olds to that in other age groups were reported for Mexico [23] and Peru [26]. During the 1967-68 influenza season in Great Britain, GP consultation rates for ILI amongst 5-14 year-olds declined during the Christmas holiday and increased when schools reopened; this effect was less clear in other age groups [17].

Winter holidays in Israel were associated with a reduction in the ratio between the number of clinic visits for influenza and those for non-respiratory complaints, in 6-12 year-olds, in three of five seasonal influenza periods studied [15]. In one season, this ratio was also reduced in adults, and in another it was reduced for adults not living with 6-12 year-olds. When a two-week teachers' strike coincided with an influenza outbreak in January 2000, closing 80% of elementary schools nationwide, this ratio decreased by 15% for 6-12 year-olds (95% CI 6-23%), but not for older individuals. As the authors note, children comprise a high proportion (34%) of the Israeli population, which may contribute to any apparent benefit of closing schools in Israel [27].

Similar data from four influenza seasons in Arizona are less consistent, partly because school closure rarely coincided with elevated influenza activity [18]. During all four seasons, rates of laboratory-confirmed influenza in school-aged children were similar during the two-week winter holiday and the preceding two weeks. In two seasons this rate increased in the two weeks after schools reopened; in one other season, it was significantly lower on reopening than during closure [18]. In comparison, rates in adults and pre-school-aged children increased successively (though not always significantly) across the three two-week periods in three of the seasons [18].

Three studies which fitted transmission models to surveillance data also concluded that school closures mainly benefit children [12 13]. Analyses of French seasonal ILI data [13] and ILI data from London during the 2009 pandemic [22] estimated that  school holidays did not affect adults' contact patterns; similarly, reductions in transmission following school closures in Hong Kong in 2009 occurred primarily amongst children [12].

However, two studies of the 2009 pandemic suggested that school closure affected incidence in adults. One of these studies estimated the age-specific number of ILI cases due to pandemic H1N1 in England; ~~in most age groups, these~~ estimated case numbers in most age groups decreased during the summer holiday and increased when schools reopened [25]. In Vojvodina, Serbia, incidence decreased amongst 5-14 and 15-64 year-olds during a one-week school closure [28].

*Reversibility of effects*

Incidence sometimes rebounded when schools reopened, suggesting that school closure contributed to reducing incidence in some settings. For example, during the 2009 pandemic in England, the estimated weekly number of infections declined during the school summer holiday; a second wave occurred when schools reopened (Supplementary Figure 2) [22 29]. Similar reversibility appeared in ILI consultation rates in Vojvodina in 2009 [28]. Datasets from the 2009 pandemic in Mexico [23 30 31] also suggested an increase in incidence after schools reopened (Supplementary Figure 2). Analyses of NPIs (usually including school closures) during the 1918 pandemic found that, in the cities studied, second waves occurred only after NPIs were lifted [5 8].

In the Israeli data regarding seasonal influenza and the teachers' strike, the number of physician visits for acute respiratory illness was 42% lower during ~~the~~ closure compared to the previous two weeks; incidence increased after the strike [27]. During the 1999-2000 influenza season in Japan, the increase in incidence appeared to slow during the two-week winter holiday and accelerated when schools reopened [7]. Similarly, in Beijing in 2009, the cumulative incidence of laboratory-confirmed H1N1 influenza increased more markedly before and after a national school holiday than during the break [32].

*Changes in transmission patterns from modelling analyses of epidemic data*

Several studies have fitted transmission models to observed epidemic data to estimate the reduction in contact rates associated with school closure. School holidays were estimated to reduce transmission of seasonal influenza amongst children by a median of 24% (range 20-29%), based on rates of ILI in France from 1985 to 2006, corresponding to a 16-18% reduction in total case numbers [13]. During the 2009 pandemic in London, contact amongst 5-14 year-olds was reduced by an estimated 72% during the six-week summer holiday; the corresponding reduction during one-week half term holidays was 48% [22]. In US cities in 1918, changes in mortality were attributed to a combination of formal interventions (including school closure) and spontaneous social distancing [8]. In Sydney in 1918, formal and spontaneous social distancing together were estimated to have reduced contact rates by up to 38% [33]. Based on influenza incidence data from the 2009 pandemic in Mexico City, school closure together with other interventions appeared to reduce the population contact rate by 23% [31]. A subsequent analysis of national data from Mexico estimated that the contact rate was reduced by 30% during the intervention period [23].

In Hong Kong (also during the 2009 pandemic), closing primary schools, kindergartens, and childcare centres pro-actively, together with affected secondary schools, was estimated to reduce transmission by 70% amongst children and 25% in the population overall [12]. The same study estimated the effective reproduction number ($R_n$, the average number of secondary infectious persons generated by a single infectious person in a given population) as 1·7 before school closure, 1·5 during school closure, and 1·1 during the subsequent school holidays [12]. Daily estimates of $R_n$ in Hong Kong in 2009 (based on a longer time series) also suggested a decline during school closure and a slight increase following reopening [34].

Modelling techniques have also been used to estimate daily values of $R_n$ during a seasonal influenza outbreak in Hong Kong [35] and the 2009 pandemic in Mexico City [23 31] and New Zealand [19]. The Hong Kong analysis for seasonal influenza suggested that $R_n$ was not substantially affected by school closure, perhaps because closure occurred late in the outbreak when $R_n$ was already below one [35]. In Mexico City [31] and New Zealand, $R_n$ was declining before schools closed and continued to decrease during closure; in New Zealand, $R_n$ increased briefly but not substantially when schools reopened [19]. Analysis of a further outbreak in the USA detected no clear effect of school closure on transmission, which was attributed to the late timing of closure [20].

Modelling analyses of the spatiotemporal spread of pandemic H1N1 in Europe in 2009 were able to reproduce observed incidence patterns only when contact rates were allowed to change specifically during each country's school holidays (holidays were assumed to eliminate transmission in schools and increase community transmission by a factor of 1.4) [36]. In all countries, holidays were estimated to delay the peak compared to a hypothetical situation without school closure. In contrast, regression analysis of estimates of $R_n$ in 12 European countries found no evidence of an effect of school holidays on transmission in the nine countries in which school holidays coincided with the study period [37]. The authors proposed that this apparent lack of effect might result from changes in reporting, stochastic effects early in the outbreaks, and the fact that in some countries (including England), school holidays occurred outside the study period.

*Different school closure strategies*

In some outbreaks, individual schools were closed; in others, school closure was more widespread (Supplementary Tables 1 and 2). The effects of these different strategies could not be compared, due to both late implementation and differences between the studies in other factors (such as the duration of closure).

Analyses of the 1918 pandemic in US cities found that the duration of NPIs was negatively associated with the total excess death rate [9]. In the datasets reviewed here, closures longer than two weeks were associated with reduced incidence or transmission in several studies of seasonal [38] and pandemic [12 29] influenza, but not in others [11 39]. Two studies which suggested reasonably strong evidence of an effect of school closure (from France and Israel) reported on closures lasting two weeks [13 27]. Studies in Japan [7] and England and Wales [17] also suggested possible effects of two-week closures on seasonal influenza. However, two-week closures ~~of this length~~ did not always appear to reduce transmission [35]. Shorter closures, e.g. of 1-2 weeks, may sometimes have contributed to reductions in transmission [22 29 31 32 40], but often had no obvious effect [41-44]. In London, contacts between children were reduced more dramatically during a six-week holiday than during one-week breaks, but this may reflect different behaviour during the different holidays [22].

*Use of multiple interventions*

In most of the pandemic influenza studies, other interventions were implemented alongside school closure and may have contributed to any reduction in incidence. In 2009, antiviral treatment and / or prophylaxis was commonly used in the studies identified [12 14 19 20 39 40 42 45-57]. Public places were sometimes closed and / or large gatherings were discouraged or restricted [16 30 31 58]. Some datasets from the 2009 pandemic included vaccination against the pandemic strain, although this was usually only available late in the study period so would not affect the included incidence data [29 32 57 59]. In 1918, school closures were often combined with other social distancing measures [5 8 9 33]; the only study included from the 1968 pandemic was a vaccine trial [60]. Of the few pandemic studies which mentioned no additional interventions, one suggested an effect of school closures: in Israel in 2009, three waves of infection corresponded to the planned closure and reopening of schools [61]. In the England and Wales data for the 2009 pandemic, other interventions (vaccination and antivirals) were used to only a limited extent; incidence still clearly declined during the school summer holiday and increased afterwards [29].

Some studies of seasonal influenza mentioned additional interventions (e.g. vaccination [62-64], prophylactic amantadine [65], hygiene promotion [38 41 66], closure of public places [38], and advice to avoid large gatherings [44]). However, some studies without additional interventions showed reductions in incidence and / or transmission during school closure [13 27].

***Discussion***

This systematic review of the effects of school closures on influenza outbreaks extends previous reviews [2 4] to include published experiences from the 2009 pandemic. The results suggest that school closure can reduce transmission of pandemic [12] and seasonal [13 27] influenza amongst schoolchildren. Many datasets, however, show no clear effect of school closure. As noted by some authors [20 43 44], this may sometimes have been because schools shut late in the outbreak (often close to or after the peak).

In some studies, incidence increased when schools reopened [5 7 8 14 22 27 29 31]. This apparent reversibility provides evidence that school closure can cause reductions in influenza incidence. In two of the studies of seasonal influenza which showed reversibility [7 27], no additional interventions (beyond usual seasonal interventions) were used. In many other datasets, multiple interventions were used, so the specific effects of school closures are difficult to isolate.

In 2009, several countries closed schools whilst in others, planned holidays coincided with outbreaks. Several datasets from this pandemic strengthen support for school closure as an intervention; however, others illustrate that benefits are not guaranteed and that timely closure may be challenging. The sensitivity of the 2009 pandemic to school closures probably reflects the ~~age-specific attack rates, which were higher in children than adults~~high attack rates in children compared to adults; outbreaks in which children are less affected might be less sensitive to school closure.

Studies presenting age-stratified data suggested that the effects of school closure on transmission were greater amongst children than adults. Few studies stratified children further, e.g. into primary and secondary school students. Older children might socialise more than younger children during school closures, so closing primary schools may have a greater effect on transmission than closing secondary schools (e.g. in Hong Kong in 2009, primary schools were closed pro-actively whilst secondary schools closed if cases occurred amongst their students [12]).

The long term effects of closing schools are unclear, as relatively few ~~of the~~ studies presented substantial data after schools reopened. For example, school closure could result in multiple peaks, potentially involving more cases than would otherwise have occurred [8]. However, a study published since this review was conducted estimated that case numbers in Alberta, Canada, could have been up to twice as high as those seen if schools had not closed for planned holidays [67]. It is difficult to compare reactive versus pro-active closures, different durations of closure, and local versus national closures as studies typically differed in several respects. ~~Age-specific data suggest that the effects of school closure are greatest among school-aged children [12 15 17 22].~~

Some studies have concluded that reopening schools after holiday periods can accelerate epidemic growth (e.g. during the 1957 [68 69] and 2009 [70] pandemics). These studies were beyond the scope of this review of the effects of closing schools ~~after~~ during outbreaks ~~have~~

~~started~~, but they suggest that extending school holidays might delay the spread of an epidemic beginning during a break.

Results from analyses of seasonal influenza may not be directly applicable to a pandemic. Schools were often closed for planned holidays rather than in response to the outbreaks; contact patterns may differ between reactive school closures [71] and holidays [72]. Extrapolating from previous pandemics may also be problematic. Modelling studies [73-75] have predicted that school closures will have the greatest effects if transmission occurs mainly amongst children. The importance of children in transmission has varied between pandemics [76]; in 2009, attack rates were higher in children than in adults, probably because of pre-existing immunity in older individuals [77]. Viral virulence will also influence individuals' responses to school closure and other interventions, e.g. spontaneous social distancing during a mild pandemic may be less dramatic than occurred in 1918. Changes in household size, contact patterns, children's behaviour and school systems since 1918, 1957 and 1968 may also limit the generalisability of experiences from these pandemics. As noted in a study of the 1918 pandemic in Connecticut, reverse causality may occur when comparing rates in cities which closed schools to those in cities which did not, if closure was a response to a particularly severe local outbreak [10].

One limitation of the datasets is that ascertainment may have changed during the outbreaks, due to changes in surveillance and care-seeking behaviour. Increases in ascertainment during an outbreak could obscure any reductions in incidence during school closures (e.g. in one study, enhanced surveillance began the day the school closed [56]). Conversely, the proportion of patients who undergo virological testing may be reduced late in an outbreak, and in some settings (e.g. New Zealand [14]) patients with ILI were discouraged from consulting GPs during the 2009 pandemic. The estimated proportion of influenza cases that were reported in Hong Kong declined to ~5% of its original value during the move from containment to mitigation during the 2009 pandemic [12]. In England, the introduction of the National Pandemic Flu Service telephone helpline coincided with the school holiday, and was estimated to have reduced the probability of GP consultation for adults with ILI from 16% to 1.8% [22].

Case definitions may not always have been well-suited to detecting any effect of school closure. For example, school absenteeism is a relatively non-specific measure, whilst laboratory specimens frequently represent severe infections (e.g. in the elderly, who may have little contact with children and therefore be relatively unaffected by school closure).

Influenza transmission is influenced by factors besides contact in schools, including temperature and absolute humidity (AH) [78-81]. Two studies which assessed the role of AH during the 2009 pandemic did not find strong evidence that it affected transmission [24 37]. The two waves seen in the UK in 2009 could be explained by changes in contact patterns during school holidays [29 82]. In a modelling study of data from Alberta, Canada, the best-fitting model included effects of temperature and school holidays on transmission, and predicted that if schools had not closed, the outbreak would have been restricted by temperature effects but would still have been 2.1 times larger than was observed in the province as a whole (1.38 and 1.54 times in the cities of Calgary and Edmonton, respectively) [67]. A study of the interplay between school calendars, AH and population susceptibility in enhancing influenza transmission concluded that high AH may prevent influenza outbreaks [79]. However, if a sufficiently high proportion of the population is susceptible, outbreaks can occur even when AH is high; the opening of schools may enhance transmission [79]. Taken together, these studies suggest that contact in schools is not the only determinant of influenza transmission, but it is one influential (and modifiable) factor.

Previous studies have ~~attempted to~~ estimated the effects of public health interventions using transmission models [8 12 20 31]. The development of such models is complicated for the datasets reviewed here, and would not necessarily have provided conclusive insight into the impact of school closures. For example, many factors are unknown and would need to be estimated or assumed for each dataset, such as the basic reproduction number, proportion of infections that were reported, the effect of other interventions, and the proportion of individuals who were immune at the start of the outbreak.

The review was limited to published studies, which could potentially introduce publication bias. However, many of the studies identified did not aim to evaluate the effects of school closure on transmission, so publication bias appears unlikely. This is supported by the apparent lack of an effect of school closure in many of the studies (including some of those which did specifically assess school closure as an intervention). A further limitation is that most papers were screened (and all data were extracted) by a single reviewer. Foreign language papers were excluded, but in most cases it was clear from the title and / or abstract (available in English) that the papers were not relevant to this review.

***Conclusions***

The available data suggest that school closures can potentially reduce transmission during an influenza outbreak, even in the absence of other interventions, although the optimal school closure strategy is unclear. The effect of school closures is larger for school-aged children than for other age groups, although there is some evidence that incidence in adults might also be reduced. During a future pandemic (or seasonal outbreaks during which schools are closed), it will be important to collect incidence data using systematic ascertainment and a consistent case definition, before, during and after school closure, to assess the effects of school closures on transmission. Analysis of comparable data from multiple outbreaks may help to overcome some of the problems with comparability and ascertainment discussed above, and clarify which features determine the effectiveness of school closures. Although timely school closures may reduce transmission, other implications of school closure (e.g. ethical and economic considerations) [4], and viral properties such as virulence, must also be considered in policy decisions, and may depend on the local context [1].

***Summary***

*Article focus*

- This systematic review assesses the effects of school closures on transmission of influenza, including data from the recent 2009 pandemic as well as from previous pandemics and seasonal outbreaks.

*Key messages*

- The available data suggest that school closure can be a useful intervention during influenza outbreaks, with the greatest benefits occurring amongst school-aged children.

*Strengths and limitations*

- We have reviewed an extensive body of literature on the effects of school closure on the incidence and transmission of influenza.
- The optimum timing and duration of closure are unclear because studies often differed in several respects, or used other interventions in addition to school closure.

*Acknowledgements*

This paper developed from a review commissioned by the UK Health Protection Agency as part of its pandemic influenza programme. We thank Nadia Inglis, Angus Nicoll and two anonymous members of the HPA's Influenza and Respiratory Virus Programme Board for helpful comments on the review. We also thank staff at the LSHTM library for assistance in locating papers.

*Funding*

This work was partially funded by the Health Protection Agency; C.J. was supported by a Research Training Fellowship from the National Institute for Health Research.

*Role of the funding source*

NIHR had no role in the design and conduct of the study; collection, analysis or interpretation of data; writing of the report; or the decision to submit the article for publication. The HPA commissioned the research.

*Access to data*

All authors had full access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

*Data sharing*

No additional data available.

*Competing interest statement*

All authors have completed the Unified Competing Interest form at http://www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: funding from NIHR and HPA; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

*Statement of authors' roles*

B.O and J.H. had the initial idea. P.M., C.J. and E.V. developed the research questions and study design. C.J. carried out the literature review and P.M. assessed any doubtful papers. C.J., P.M. and E.V. analysed data. C.J., P.M. and E.V. wrote the paper. J.H. commented on outputs and contributed to the final draft. J.H. and B.O. contributed to the final draft.

*Ethical approval*

Not required.

### *References*

1. World Health Organization. Reducing transmission of pandemic (H1N1) 2009 in school settings. A framework for national and local planning and response, 2009.
2. Bell DM, World Health Organization Writing Group. Non-pharmaceutical interventions for pandemic influenza, national and community measures. *Emerg Infect Dis* 2006;12(1):88-94.
3. Aledort JE, Lurie N, Wasserman J, Bozzette SA. Non-pharmaceutical public health interventions for pandemic influenza: an evaluation of the evidence base. *BMC Public Health* 2007;7:208.
4. Cauchemez S, Ferguson NM, Wachtel C, Tegnell A, Saour G, Duncan B, et al. Closure of schools during an influenza pandemic. *The Lancet Infectious Diseases* 2009;9(8):473-81.
5. Hatchett RJ, Mecher CE, Lipsitch M. Public health interventions and epidemic intensity during the 1918 influenza pandemic. *Proc Natl Acad Sci U S A* 2007;104(18):7582-7.
6. Olson JG. School absenteeism during an outbread of B/Hong Kong/5/72-like influenze virus in Taipei, Taiwan. *Southeast Asian J Trop Med Public Health* 1980;11(4):429-34.
7. Fujii H, Takahashi H, Ohyama T, Hattori K, Suzuki S. Evaluation of the school health surveillance system for influenza, Tokyo, 1999-2000. *Japanese Journal of Infectious Diseases* 2002;55(3):97-98.
8. Bootsma MC, Ferguson NM. The effect of public health measures on the 1918 influenza pandemic in U.S. cities. *Proc Natl Acad Sci U S A* 2007;104(18):7588-93.
9. Markel H, Lipman HB, Navarro JA, Sloan A, Michalsen JR, Stern AM, et al. Nonpharmaceutical interventions implemented by US cities during the 1918-1919 influenza pandemic.[Erratum appears in JAMA. 2007 Nov 21;298(19):2264]. *Jama* 2007;298(6):644-54.
10. Winslow C-EA, Rogers JF. Statistics of the 1918 Epidemic of Influenza in Connecticut: With a consideration of the factors which influenced the prevalence of this disease in various communities *J Infect Dis* 1920;26(3):185-216.
11. Armstrong C, Hopkins R. An epidemiological study of the 1920 epidemic of influenza in an isolated rural community. *Public Health Reports* 1921;36(29):1671-702.
12. Wu JT, Cowling BJ, Lau EH, Ip DK, Ho LM, Tsang T, et al. School closure and mitigation of pandemic (H1N1) 2009, Hong Kong. *Emerg Infect Dis* 2010;16(3):538-41.
13. Cauchemez S, Valleron A-J, Boelle P-Y, Flahault A, Ferguson NM. Estimating the impact of school closure on influenza transmission from Sentinel data. *Nature* 2008;452(7188):750-4.
14. Baker MG, Wilson N, Huang QS, Paine S, Lopez L, Bandaranayake D, et al. Pandemic influenza A(H1N1)v in New Zealand: the experience from April to August 2009. *Euro Surveill* 2009;14(34).
15. Heymann AD, Hoch I, Valinsky L, Kokia E, Steinberg DM. School closure may be effective in reducing transmission of respiratory viruses in the community. *Epidemiol Infect* 2009;137(10):1369-76.
16. Tinoco Y, Razuri H, Ortiz EJ, Gomez J, Widdowson MA, Uyeki T, et al. Preliminary population-based epidemiological and clinical data on 2009 pandemic H1N1 influenza A (pH1N1) from Lima, Peru. *Influenza Other Respi Viruses* 2009;3(6):253-6.
17. Miller DL, Lee JA. Influenza in Britain 1967-68. *Journal of Hygiene* 1969;67:559-72.

18. Wheeler CC, Erhart LM, Jehn ML. Effect of school closure on the incidence of influenza among school-age children in Arizona. *Public Health Rep* 2010;125(6):851-9.
19. Paine S, Mercer GN, Kelly PM, Bandaranayake D, Baker MG, Huang QS, et al. Transmissibility of 2009 pandemic influenza A(H1N1) in New Zealand: effective reproduction number and influence of age, ethnicity and importations. *Euro Surveill* 2010;15(24).
20. Cauchemez S, Bhattarai A, Marchbanks TL, Fagan RP, Ostroff S, Ferguson NM, et al. Role of social networks in shaping disease transmission during a community outbreak of 2009 H1N1 pandemic influenza. *Proc Natl Acad Sci U S A* 2011;108(7):2825-30.
21. Marchbanks TL, Bhattarai A, Fagan RP, Ostroff S, Sodha SV, Moll ME, et al. An outbreak of 2009 pandemic influenza A (H1N1) virus infection in an elementary school in Pennsylvania. *Clin Infect Dis* 2011;52 Suppl 1:S154-60.
22. Birrell PJ, Ketsetzis G, Gay NJ, Cooper BS, Presanis AM, Harris RJ, et al. Bayesian modeling to unmask and predict influenza A/H1N1pdm dynamics in London. *Proceedings of the National Academy of Sciences of the United States of America* 2011;108(45):18238-43.
23. Chowell G, Echevarria-Zuno S, Viboud C, Simonsen L, Tamerius J, Miller MA, et al. Characterizing the epidemiology of the 2009 influenza A/H1N1 pandemic in Mexico. *PLoS Med* 2011;8(5):e1000436.
24. Chowell G, Viboud C, Munayco CV, Gomez J, Simonsen L, Miller MA, et al. Spatial and temporal characteristics of the 2009 A/H1N1 influenza pandemic in Peru. *PLoS ONE* 2011;6(6):e21287.
25. Evans B, Charlett A, Powers C, McLean E, Zhao H, Bermingham A, et al. Has estimation of numbers of cases of pandemic influenza H1N1 in England in 2009 provided a useful measure of the occurrence of disease? *Influenza and other Respiratory Viruses* 2011;5(6):e504-e12.
26. Munayco CV, Gomez J, Laguna-Torres VA, Arrasco J, Kochel TJ, Fiestas V, et al. Epidemiological and transmissibility analysis of influenza A(H1N1)v in a southern hemisphere setting: Peru. *Euro surveillance : bulletin europeen sur les maladies transmissibles = European communicable disease bulletin* 2009;14(32).
27. Heymann A, Chodick G, Reichman B, Kokia E, Laufer J. Influence of school closure on the incidence of viral respiratory diseases among children and on health care utilization. *Pediatr Infect Dis J* 2004;23(7):675-7.
28. Petrovic V, Seguljev Z, Cosic G, Ristic M, Nedeljkovic J, Dragnic N, et al. Overview of the winter wave of 2009 pandemic influenza A(H1N1)v in Vojvodina, Serbia. *Croatian Medical Journal* 2011;52(2):141-50.
29. Baguelin M, Hoek AJV, Jit M, Flasche S, White PJ, Edmunds WJ. Vaccination against pandemic influenza A/H1N1v in England: A real-time economic evaluation. *Vaccine* 2010;28(12):2370-84.
30. Echevarria-Zuno S, Mejia-Arangure JM, Mar-Obeso AJ, Grajales-Muniz C, Robles-Perez E, Gonzalez-Leon M, et al. Infection and death from influenza A H1N1 virus in Mexico: a retrospective analysis. *Lancet* 2009.
31. Cruz-Pacheco G, Duran L, Esteva L, Minzoni A, Lopez-Cervantes M, Panayotaros P, et al. Modelling of the influenza A(H1N1)v outbreak in Mexico City, April-May 2009, with control sanitary measures. *Euro Surveill* 2009;14(26).
32. Wu J, Xu F, Lu L, Lu M, Miao L, Gao T, et al. Safety and effectiveness of a 2009 H1N1 vaccine in Beijing. *New England Journal of Medicine* 2010;363(25):2416-23.
33. Caley P, Philp DJ, McCracken K. Quantifying social distancing arising from pandemic influenza. *Journal of the Royal Society Interface* 2008;5(23):631-9.

34. Cowling BJ, Lau MSY, Ho LM, Chuang SK, Tsang T, Liu SH, et al. The effective reproduction number of pandemic influenza: Prospective estimation. *Epidemiology* 2010;21(6):842-46.
35. Cowling BJ, Lau EHY, Lam CLH, Cheng CKY, Kovar J, Chan KH, et al. Effects of school closures, 2008 winter influenza season, Hong Kong. *Emerg Infect Dis* 2008;14(10):1660-2.
36. Merler S, Ajelli M, Pugliese A, Ferguson NM. Determinants of the spatiotemporal dynamics of the 2009 H1N1 pandemic in europe: Implications for real-time modelling. *PLoS Computational Biology* 2011;7(9).
37. Flasche S, Hens N, Boëlle P-Y, Mossong J, van Ballegooijen WM, Nunes B, et al. Different transmission patterns in the early stages of the influenza A(H1N1)v pandemic: A comparative analysis of 12 European countries. *Epidemics* 2011;3(2):125-33.
38. Lo JY, Tsang TH, Leung YH, Yeung EY, Wu T, Lim WW. Respiratory infections during SARS outbreak, Hong Kong, 2003. *Emerg Infect Dis* 2005;11(11):1738-41.
39. Gomez J, Munayco C, Arrasco J, Suarez L, Laguna-Torres V, Aguilar P, et al. Pandemic influenza in a southern hemisphere setting: the experience in Peru from May to September, 2009. *Euro Surveillance: Bulletin Europeen sur les Maladies Transmissibles = European Communicable Disease Bulletin* 2009;14(42).
40. Kawaguchi R, Miyazono M, Noda T, Takayama Y, Sasai Y, Iso H. Influenza (H1N1) 2009 outbreak and school closure, Osaka Prefecture, Japan. *Emerg Infect Dis* 2009;15(10):1685.
41. Danis K, Fitzgerald M, Connell J, Conlon M, Murphy PG. Lessons from a pre-season influenza outbreak in a day school. *Commun Dis Public Health* 2004;7(3):179-83.
42. Calatayud L, Kurkela S, Neave PE, Brock A, Perkins S, Zuckerman M, et al. Pandemic (H1N1) 2009 virus outbreak in a school in London, April-May 2009: an observational study. *Epidemiol Infect* 2010;138(2):183-91.
43. Rodriguez CV, Rietberg K, Baer A, Kwan-Gett T, Duchin J. Association between school closure and subsequent absenteeism during a seasonal influenza epidemic. *Epidemiology* 2009;20(6):787-92.
44. Johnson AJ, Moore ZS, Edelson PJ, Kinnane L, Davies M, Shay DK, et al. Household responses to school closure resulting from outbreak of influenza B, North Carolina. *Emerg Infect Dis* 2008;14(7):1024-30.
45. Smith A, Coles S, Johnson S, Saldana L, Ihekweazu C, O'Moore E. An outbreak of influenza A(H1N1)v in a boarding school in South East England, May-June 2009. *Euro Surveill* 2009;14(27):9.
46. Effler PV, Carcione D, Giele C, Dowse GK, Goggin L, Mak DB. Household responses to pandemic (H1N1) 2009-related school closures, Perth, Western Australia. *Emerg Infect Dis* 2010;16(2):205-11.
47. Health Protection Agency West Midlands H1N1v Investigation Team. Preliminary descriptive epidemiology of a large school outbreak of influenza A(H1N1)v in the West Midlands, United Kingdom, May 2009. *Euro Surveill* 2009;14(27).
48. Wallensten A, Oliver I, Lewis D, Harrison S. Compliance and side effects of prophylactic oseltamivir treatment in a school in South West England. *Euro Surveill* 2009;14(30):19285.
49. Strong M, Burrows J, Stedman E, Redgrave P. Adverse drug effects following oseltamivir mass treatment and prophylaxis in a school outbreak of 2009 pandemic influenza A(H1N1) in June 2009, Sheffield, United Kingdom. *Euro Surveill* 2010;15(19):pii/19565.

50. Guinard A, Grout L, Durand C, Schwoebel V. Outbreak of influenza A(H1N1)v without travel history in a school in the Toulouse district, France, June 2009. *Euro Surveill* 2009;14(27).
51. France AM, Jackson M, Schrag S, Lynch M, Zimmerman C, Biggerstaff M, et al. Household transmission of 2009 influenza A (H1N1) virus after a school-based outbreak in New York City, April-May 2009. *J Infect Dis* 2010;201(7):984-92.
52. Lessler J, Reich NG, Cummings DAT, New York City Department of H, Mental Hygiene Swine Influenza Investigation T, Nair HP, et al. Outbreak of 2009 pandemic influenza A (H1N1) at a New York City school. *N Engl J Med* 2009;361(27):2628-36.
53. Nishiura H, Castillo-Chavez C, Safan M, Chowell G. Transmission potential of the new influenza A(H1N1) virus and its age-specificity in Japan. *Euro Surveill* 2009;14(22):4.
54. Shimada T, Gu Y, Kamiya H, Komiya N, Odaira F, Sunagawa T, et al. Epidemiology of influenza A(H1N1)v virus infection in Japan, May-June 2009. *Euro Surveill* 2009;14(24).
55. Carrillo-Santisteve P, Renard-Dubois S, Cheron G, Csaszar-Goutchkoff M, Lecuit M, Lortholary O, et al. 2009 pandemic influenza A(H1N1) outbreak in a complex of schools in Paris, France, June 2009. *Euro Surveill* 2010;15(25):24.
56. Huai Y, Lin J, Varma JK, Peng Z, He J, Cheng C, et al. A primary school outbreak of pandemic 2009 influenza A (H1N1) in China. *Influenza other respi* 2010;4(5):259-66.
57. Poggensee G, Gilsdorf A, Buda S, Eckmanns T, Claus H, Altmann D, et al. The first wave of pandemic influenza (H1N1) 2009 in Germany: From initiation to acceleration. *BMC Infectious Diseases* 2010;10(155).
58. Miller JC, Danon L, O'Hagan JJ, Goldstein E, Lajous M, Lipsitch M. Student behavior during a school closure caused by pandemic influenza A/H1N1. *PLoS ONE* 2010;5(5):e10425.
59. Hsueh P-R, Lee P-I, Hsiang Chiu A-W, Yen M-Y. Pandemic (H1N1) 2009 vaccination and class suspensions after outbreaks, Taipei City, Taiwan. *Emerg Infect Dis* 2010;16(8):1309-11.
60. Monto AS, Davenport FM, Napier JA, Francis Jr T. Modification of an outbreak of influenza in tecumseh, michigan by vaccination of schookhildren. *J.Infect.Dis* 1970;122(1-2):328-32.
61. Engelhard D, Bromberg M, Averbuch D, Tenenbaum A, Goldmann D, Kunin M, et al. Increased extent of and risk factors for pandemic (H1N1) 2009 and seasonal infl uenza among children, Israel. *Emerging Infectious Diseases* 2011;17(9):1740-43.
62. Briscoe JH. The protective effect of influenza vaccine in a mixed influenza A and B epidemic in a boys' boarding school. *J R Coll Gen Pract* 1977;27(166):28-31.
63. Farley TA, St. Germain JM, Chamberlain LA, Krassner L. The impact of influenza vaccination on respiratory illness at a boarding School. *Journal of American College Health* 1992;41(3):127-31.
64. Sonoguchi T, Naito H, Hara M. Cross-subtype protection in humans during sequential, overlapping, and/or concurrent epidemics caused by H3N2 and H1N1 influenza viruses. *Journal of Infectious Diseases* 1985;151(1):81-88.
65. Davies JR, Grilli EA, Smith AJ, Hoskins TW. Prophylactic use of amantadine in a boarding school outbreak of influenza A. *J R Coll Gen Pract* 1988;38(313):346-8.
66. Cashman P, Massey P, Durrheim D, Islam F, Merritt T, Eastwood K. Pneumonia cluster in a boarding school--implications for influenza control. *Commun Dis Intell* 2007;31(3):296-8.

67. Earn DJ, He D, Loeb MB, Fonseca K, Lee BE, Dushoff J. Effects of school closure on incidence of pandemic influenza in Alberta, Canada. *Ann Intern Med* 2012;156(3):173-81.
68. Brunyate WDT, Fleming GM, Llopis A, Roden AT. The early stages of the 1957 influenza epidemic in England and Wales in relation to the re-assembly of schools. *Mon Bull Minist Hlth Lab Serv* 1961;20(MAY):88-92.
69. Dunn FL, Carey DE, Cohen A, Martin JD. Epdemiologic studies of asian influenza in a louisiana parish. *Amer* 1959;J.Hyg. 70(3):351-71.
70. Chao DL, Halloran ME, Longini IM, Jr. School opening dates predict pandemic influenza A(H1N1) outbreaks in the United States. *J Infect Dis* 2010;202(6):877-80.
71. Jackson C, Mangtani P, Vynnycky E, Fielding K, Kitching A, Mohamed H, et al. School Closures and Student Contact Patterns. *Emerg Infect Dis* 2011;17(2):245-47.
72. Eames KTD, Tilston NL, White PJ, Adams E, Edmunds WJ. The impact of illness and the impact of school closure on social contact patterns. *Health Technol Assess* 2010;14(34):267-312.
73. Glass K, Barnes B. How much would closing schools reduce transmission during an influenza pandemic? *Epidemiology* 2007;18(5):623-8.
74. Vynnycky E, Edmunds WJ. Analyses of the 1957 (Asian) influenza pandemic in the United Kingdom and the impact of school closures. *Epidemiol Infect* 2008;136(2):166-79.
75. Milne GJ, Kelso JK, Kelly HA, Huband ST, McVernon J. A small community model for the transmission of infectious diseases: comparison of school closure as an intervention in individual-based models of an influenza pandemic. *PLoS ONE* 2008;3(12):e4005.
76. Davis LE, Caldwell GG, Lynch RE. Hong Kong influenza: The epidemiologic features of a high school family study analyzed and compared with a similar study during the 1957Asian influenza epidemic. *American Journal of Epidemiology* 1970;92(4):520.
77. Miller E, Hoschler K, Hardelid P, Stanford E, Andrews N, Zambon M. Incidence of 2009 pandemic influenza A H1N1 infection in England: a cross-sectional serological study. *Lancet* 2010;375(9720):1100-8.
78. Lowen AC, Mubareka S, Steel J, Palese P. Influenza Virus Transmission Is Dependent on Relative Humidity and Temperature. *PLoS Pathog* 2007;3(10):e151.
79. Shaman J, Goldstein E, Lipsitch M. Absolute humidity and pandemic versus epidemic influenza. *Am J Epidemiol* 2011;173(2):127-35.
80. Shaman J, Kohn M. Absolute humidity modulates influenza survival, transmission, and seasonality. *Proc Natl Acad Sci U S A* 2009;106(9):3243-8.
81. Shaman J, Pitzer VE, Viboud C, Grenfell BT, Lipsitch M. Absolute humidity and the seasonal onset of influenza in the continental United States. *PLoS Biol* 2010;8(2):e1000316.
82. Eames KT, Tilston NL, Brooks-Pollock E, Edmunds WJ. Measured Dynamic Social Contact Patterns Explain the Spread of H1N1v Influenza. *PLoS Comput Biol* 2012;8(3):e1002425.
83. Uchida M, Tsukahara T, Kaneko M, Washizuka S, Kawa S. Swine-origin influenza a outbreak 2009 at Shinshu University, Japan. *BMC Public Health* 2011;11:79.

**Table 1:** Features of the studies identified. Studies may present more than one dataset and so appear in more than one row of each section.

| | | Number of studies |
|---|---|---|
| | ***Total studies*** | ***79*** |
| Type of outbreak | Seasonal | 22 |
| | 1918 pandemic | 7 |
| | 1968 pandemic | 1 |
| | 2009 pandemic | 49 |
| Setting | Europe | 22 |
| | North America | 22 |
| | Central America | 5 |
| | South America | 3 |
| | Asia | 20 |
| | Africa | 1 |
| | Australasia | 6 |
| Data provided on[1]: | Children only | 25 |
| | General population | 29 |
| | School pupils and staff | 5 |
| | Children and other specified groups separately | 22 |
| Reason for closure | High student absenteeism | 3 |
| | High staff absenteeism | 1 |
| | High student and staff absenteeism | 1 |
| | Other reactive closure[2] | 31 |
| | Pro-active | 7 |
| | Planned holiday | 38 |
| | Other[3] | 3 |
| | Unclear | 3 |
| Period of closure | Continuous | 67 |
| | Intermittent | 8 |
| | Variable[4] | 3 |
| | Not stated | 1 |
| Other interventions in place[5] | None | 20 |
| | Antivirals | 33 |
| | Other social distancing | 24 |
| | Vaccination | 8 |
| | Other | 20 |
| Timing of closure | Before peak | 21 |
| | Same day / week as peak | 9 |
| | After peak | 36 |
| | Variable[4] | 8 |
| | Unclear | 8 |
| Duration of closure[6] | <7 days | 8 |
| | 7-13 days | 33 |
| | 14-20 days | 19 |
| | ≥21 days | 17 |
| | Variable[4] | 6 |
| | Not stated | 2 |

[1] Each study may present more than one data source

[2] Closure in response to outbreak, not stated as being for operational reasons

[3] Teachers' strike (2 studies) or response to SARS outbreak (1 study)

[4] Studies of multiple US cities during the 1918 pandemic or multiple countries in 2009

[5] Described in the included paper or related papers; excludes normal levels of vaccine and antiviral usage in seasonal datasets.

[6] Each study may present more than one dataset for which the durations of closure differed

***Figure legends***

**Figure 1:** Identification of epidemiological studies of the effects of school closure on influenza outbreaks

**Figure 2:** Peak cumulative attack rates recorded in the identified studies. Case definitions varied between studies (see Appendix); only studies which included a denominator are shown. Studies which reported peak prevalence of absenteeism are denoted by an asterisk. See Appendix for full details of datasets. Abbreviations: BC, British Colombia; IL, Illinois; CT, Connecticut; NC, North Carolina; UK, United Kingdom; KI, Kelleys Island. All pandemic data are from 2009 except for Kelleys Island.

**Figure 3:** Normalised peak attack rates (estimated as peak attack rate / median attack rate) recorded in the identified studies; one study with an estimate normalised peak of 128 is excluded for clarity [83]. Case definitions varied between studies (see Appendix). Studies which reported peak prevalence of absenteeism are denoted by an asterisk. Abbreviations: HK, Hong Kong; IL, Illinois; SARI, severe acute respiratory infection; NC, North Carolina; UK, United Kingdom; KI, Kelleys Island.

**Box 1: Information extracted from eligible studies (where presented)**

Study design

Study population / setting (including size of population)

Nature of school closure (e.g. school holiday, response to outbreak)

Duration of closure and number of schools affected

Timing of closure in relation to influenza circulation

Outcome measure(s) examined (e.g. clinical ILI, virologically confirmed influenza)

Association between school closure and outcome

Epidemic curve (transcribed from graphs or figures); used to derive peak, cumulative and median attack rates

Normalised peak attack rate (= peak attack rate / median attack rate)

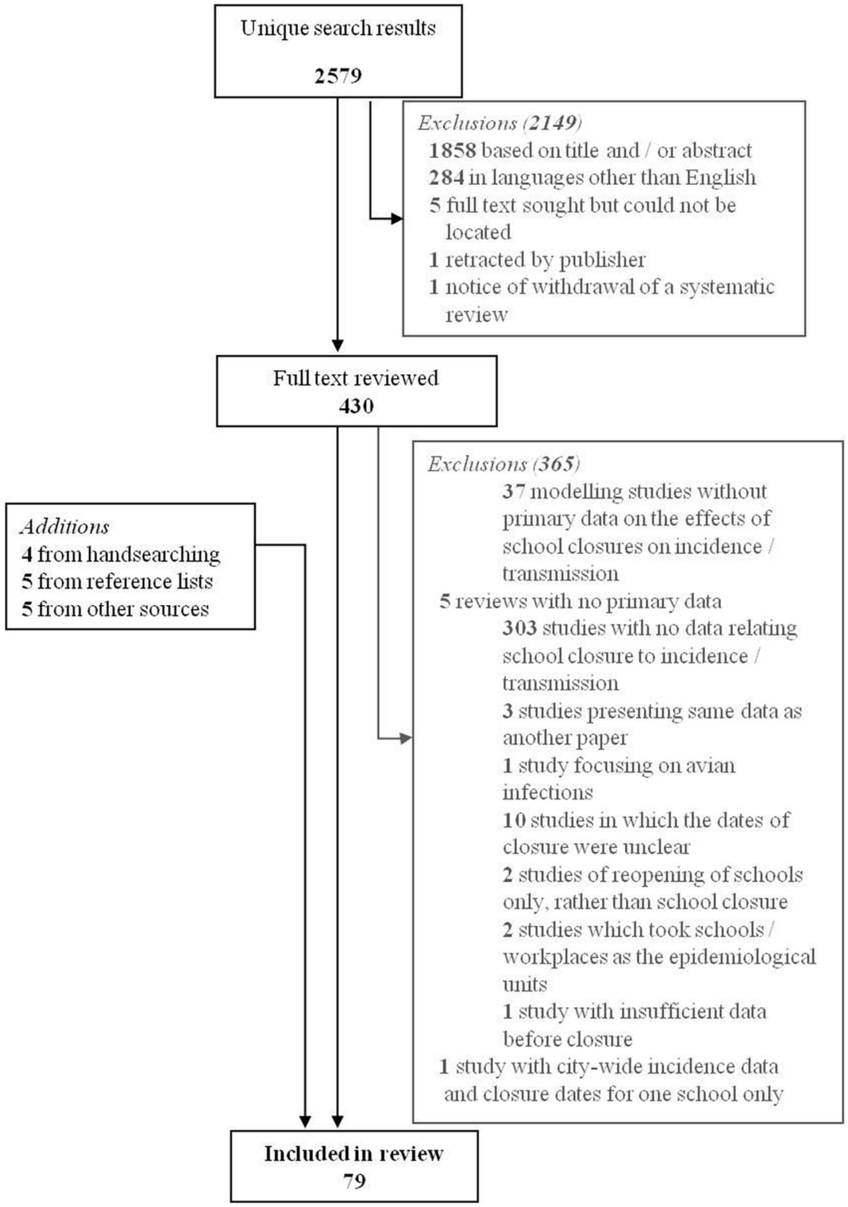



Figure 1: Identification of epidemiological studies of the effects of school closure on influenza outbreaks
90x128mm (300 x 300 DPI)

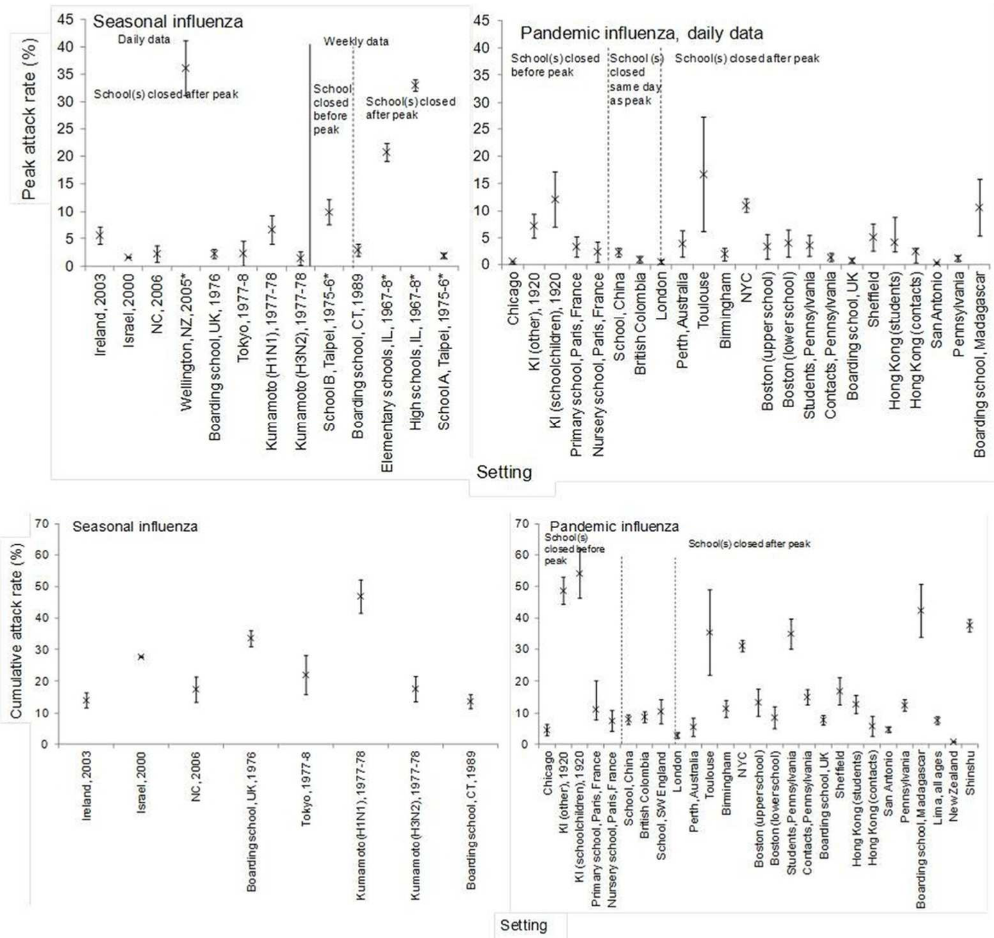



Figure 2: Peak cumulative attack rates recorded in the identified studies. Case definitions varied between studies (see Appendix); only studies which included a denominator are shown. Studies which reported peak prevalence of absenteeism are denoted by an asterisk. See Appendix for full details of datasets. Abbreviations: BC, British Colombia; IL, Illinois; CT, Connecticut; NC, North Carolina; UK, United Kingdom; KI, Kelleys Island. All pandemic data are from 2009 except for Kelleys Island.
95x90mm (300 x 300 DPI)

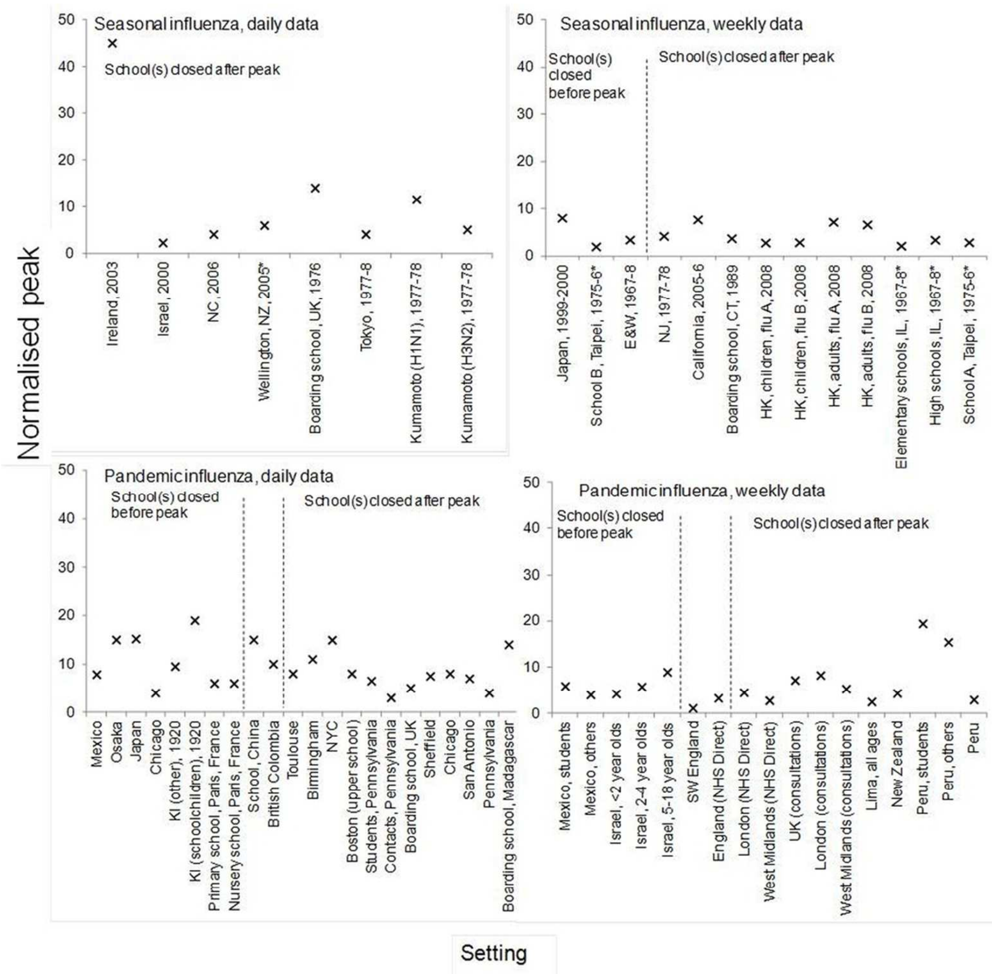



Figure 3: Normalised peak attack rates (estimated as peak attack rate / median attack rate) recorded in the identified studies; one study with an estimate normalised peak of 128 is excluded for clarity 83. Case definitions varied between studies (see Appendix). Studies which reported peak prevalence of absenteeism are denoted by an asterisk. Abbreviations: HK, Hong Kong; IL, Illinois; SARI, severe acute respiratory infection; NC, North Carolina; UK, United Kingdom; KI, Kelleys Island.
91x90mm (300 x 300 DPI)

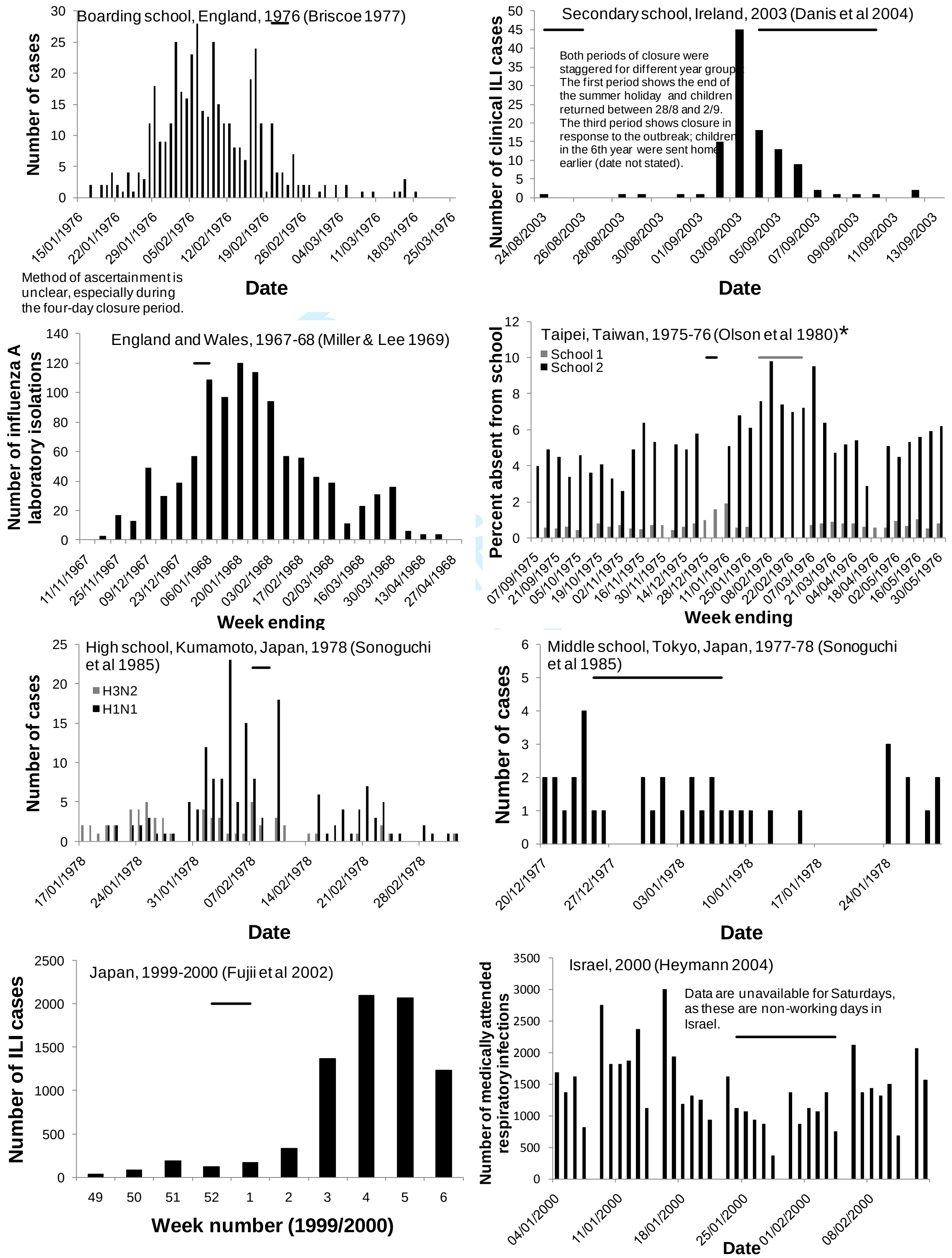
**Epidemiological evidence of the effects of school closures on influenza outbreaks: systematic review**

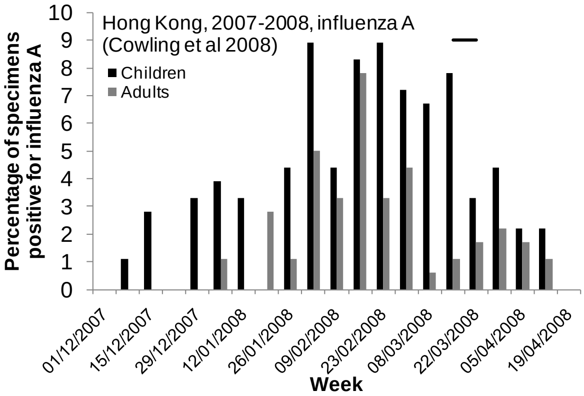
**Supplementary Information**

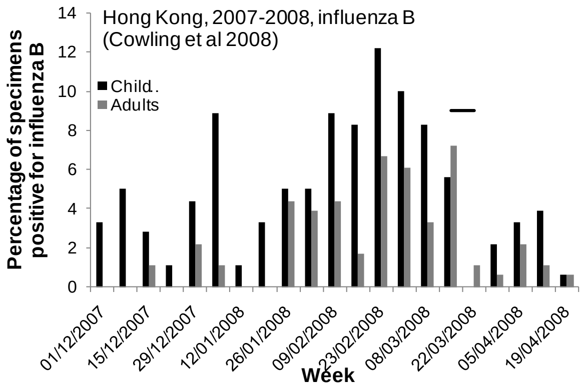
**Search strategy used in Medline**

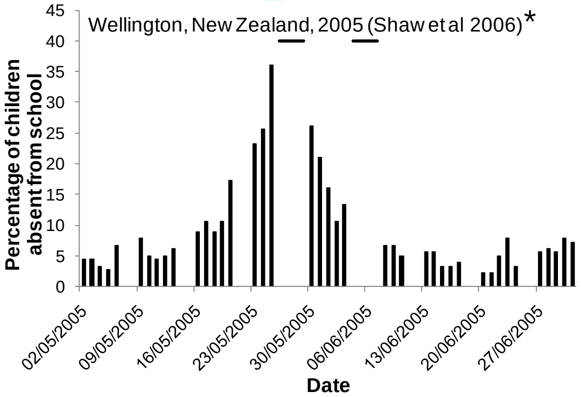
1. influenza.mp. or exp Influenza, Human/
2. exp Incidence/
3. exp Morbidity/
4. exp Sentinel Surveillance/ or exp Population Surveillance/
5. exp Disease Transmission, Horizontal/ or exp Acute Disease/ or exp Disease Notification/ or exp Disease Outbreaks/ or exp Communicable Disease Control/ or exp Disease/ or exp Disease Transmission/
6. (incidence or rate or morbidity or mortality or surveillance or risk or illness or death or case* or disease or infect*).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
7. (infect* or communicable or contagio*).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
8. exp Infection/
9. exp Communicable Diseases/ or exp Communicable Disease Control/ or exp Communicable Diseases, Emerging/
10. 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. ((school adj5 clos*) or (nurser* adj5 clos*) or (daycare adj5 clos*) or (day adj care adj5 clos*)).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
12. exp Schools/
13. 11 or 12
14. 1 and 10 and 13

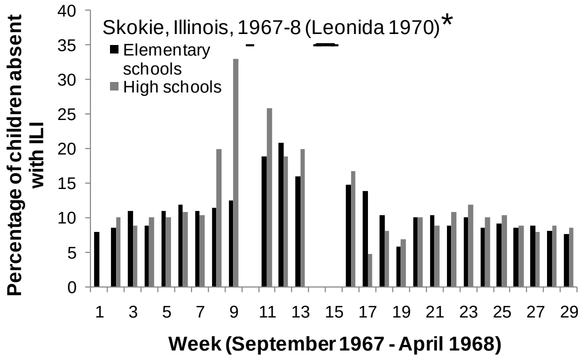
Supplementary Figure 1: Epidemic curves for seasonal influenza. Horizontal lines show periods of school closure (weekends are shown only if they are continuous with periods of pro-active or reactive closure). Data are daily unless the x axis indicates otherwise. See Supplementary Table 1 for case definitions and full details of the datasets. School absenteeism data are denoted by an asterisk.

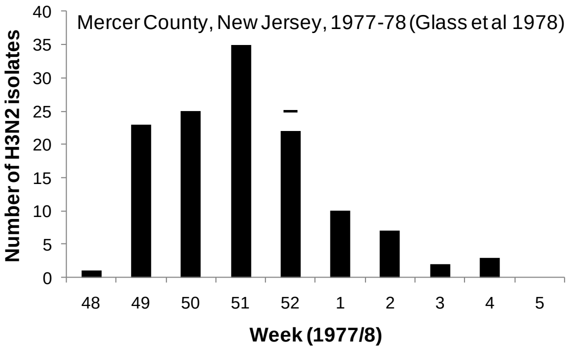


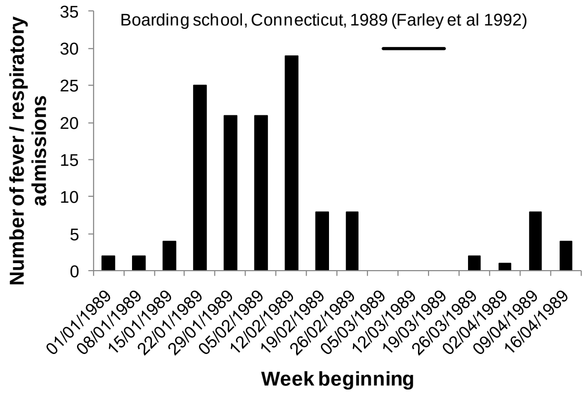

Hong Kong, 2007-2008, influenza A
(Cowling et al 2008)
Children
Adults
Percentage of specimens positive for influenza A
Week

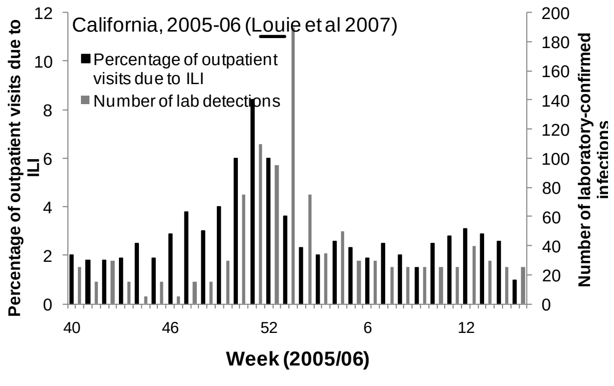

Hong Kong, 2007-2008, influenza B
(Cowling et al 2008)
Adults
Percentage of specimens positive for influenza B
Week

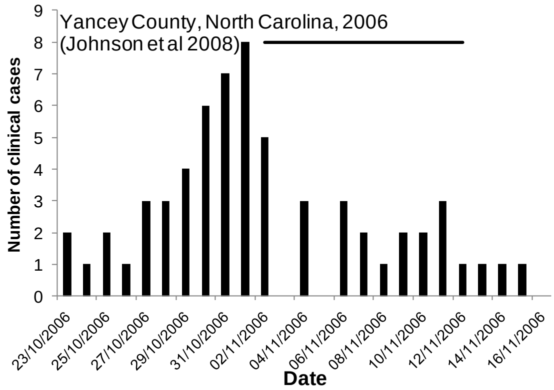

Wellington, New Zealand, 2005 (Shaw et al 2006)*
Percentage of children absent from school
Date


Skokie, Illinois, 1967-8 (Leonida 1970)*
Elementary schools
High schools
Percentage of children absent with ILI
Week (September 1967 - April 1968)

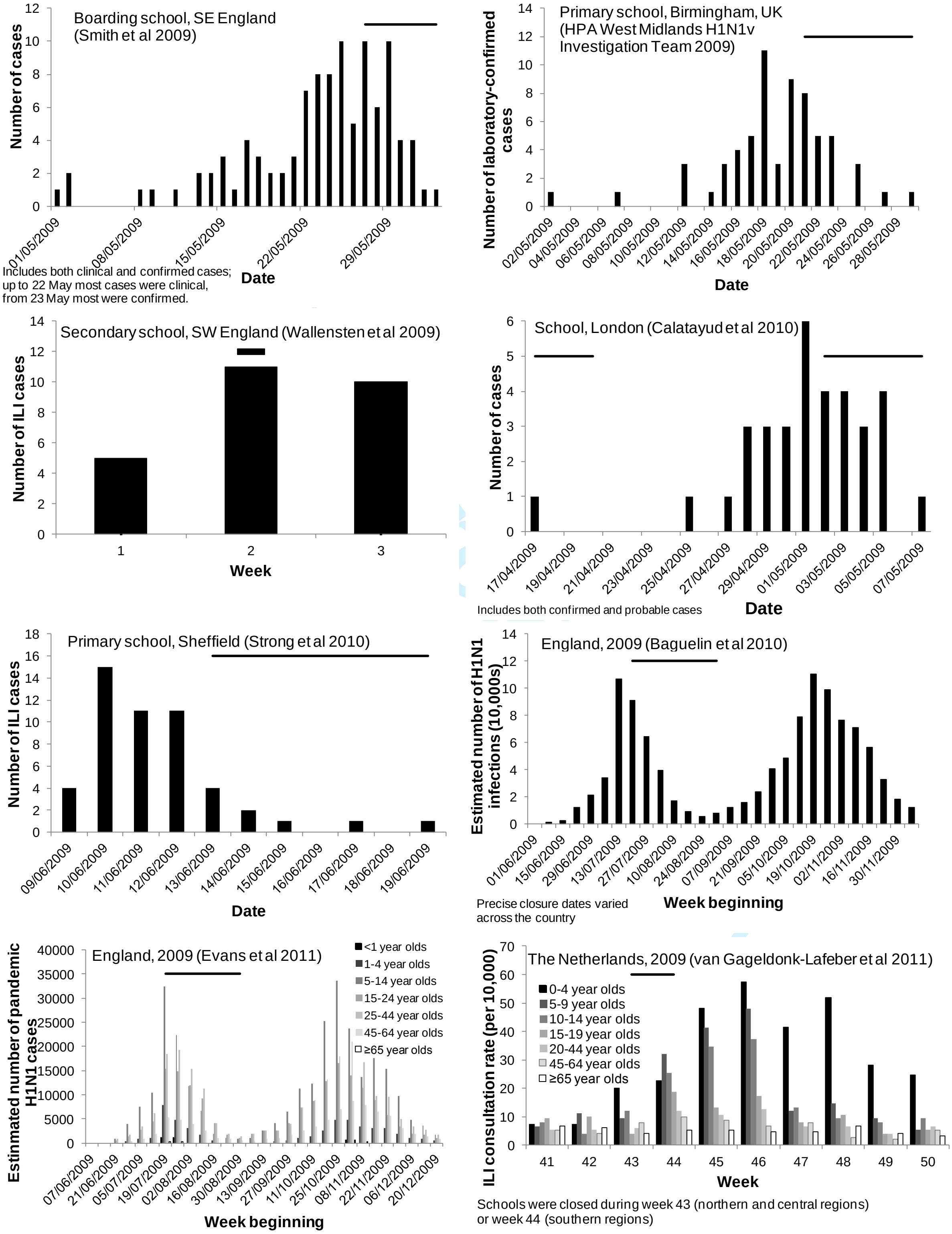

Mercer County, New Jersey, 1977-78 (Glass et al 1978)
Number of H3N2 isolates
Week (1977/8)

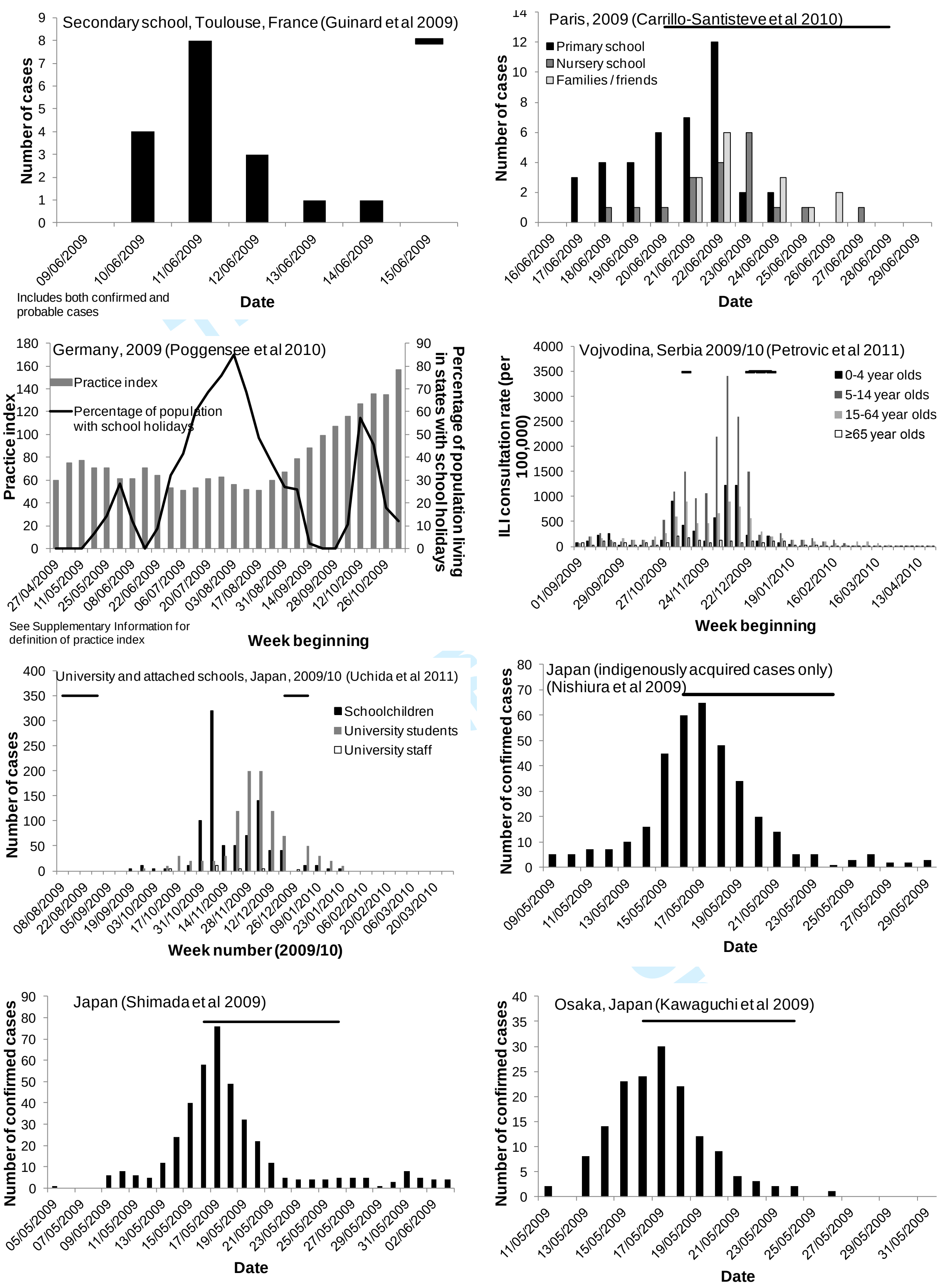

Boarding school, Connecticut, 1989 (Farley et al 1992)
Number of fever / respiratory admissions
Week beginning

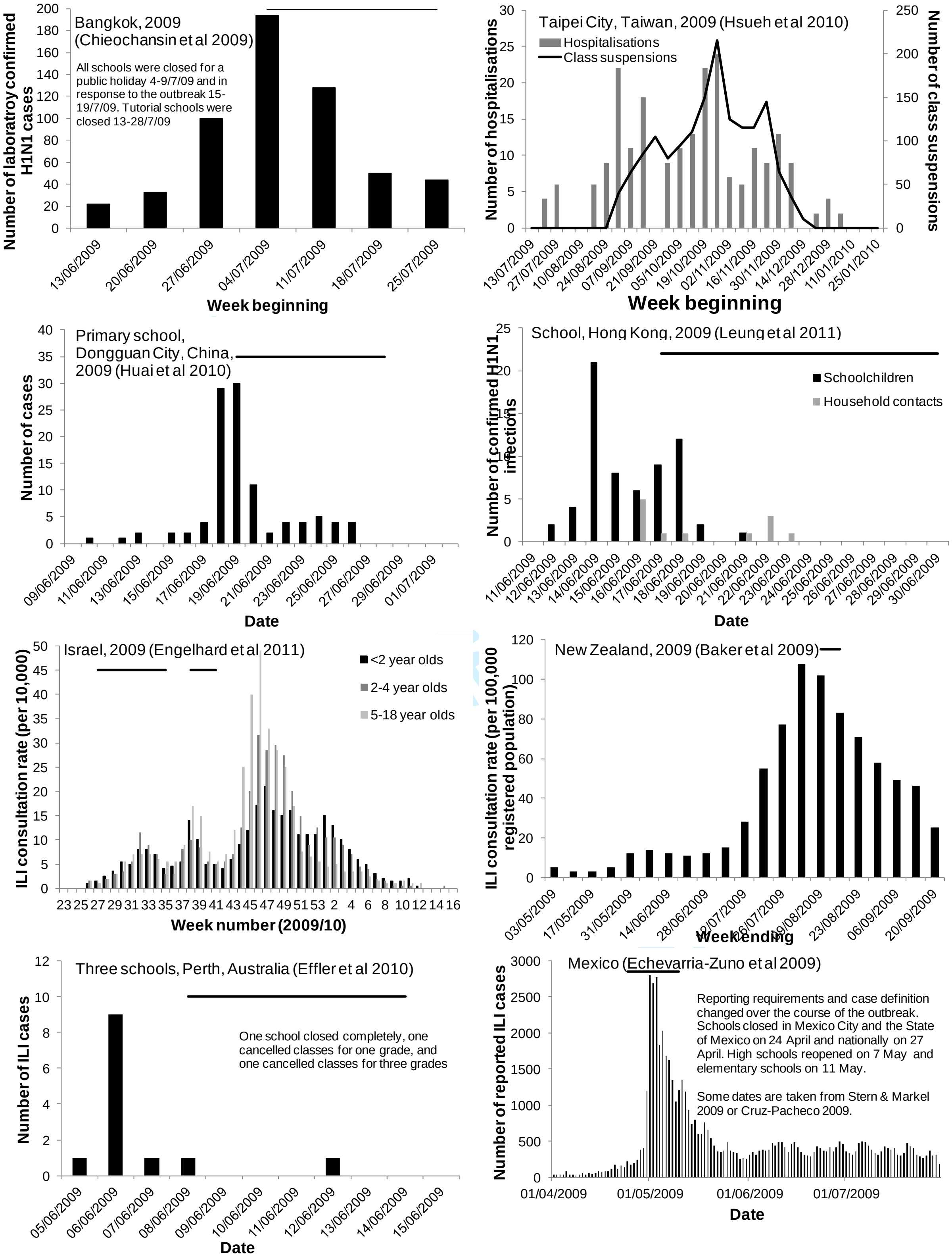

California, 2005-06 (Louie et al 2007)
Percentage of outpatient visits due to ILI
Number of lab detections
Percentage of outpatient visits due to ILI
Number of laboratory-confirmed infections
Week (2005/06)

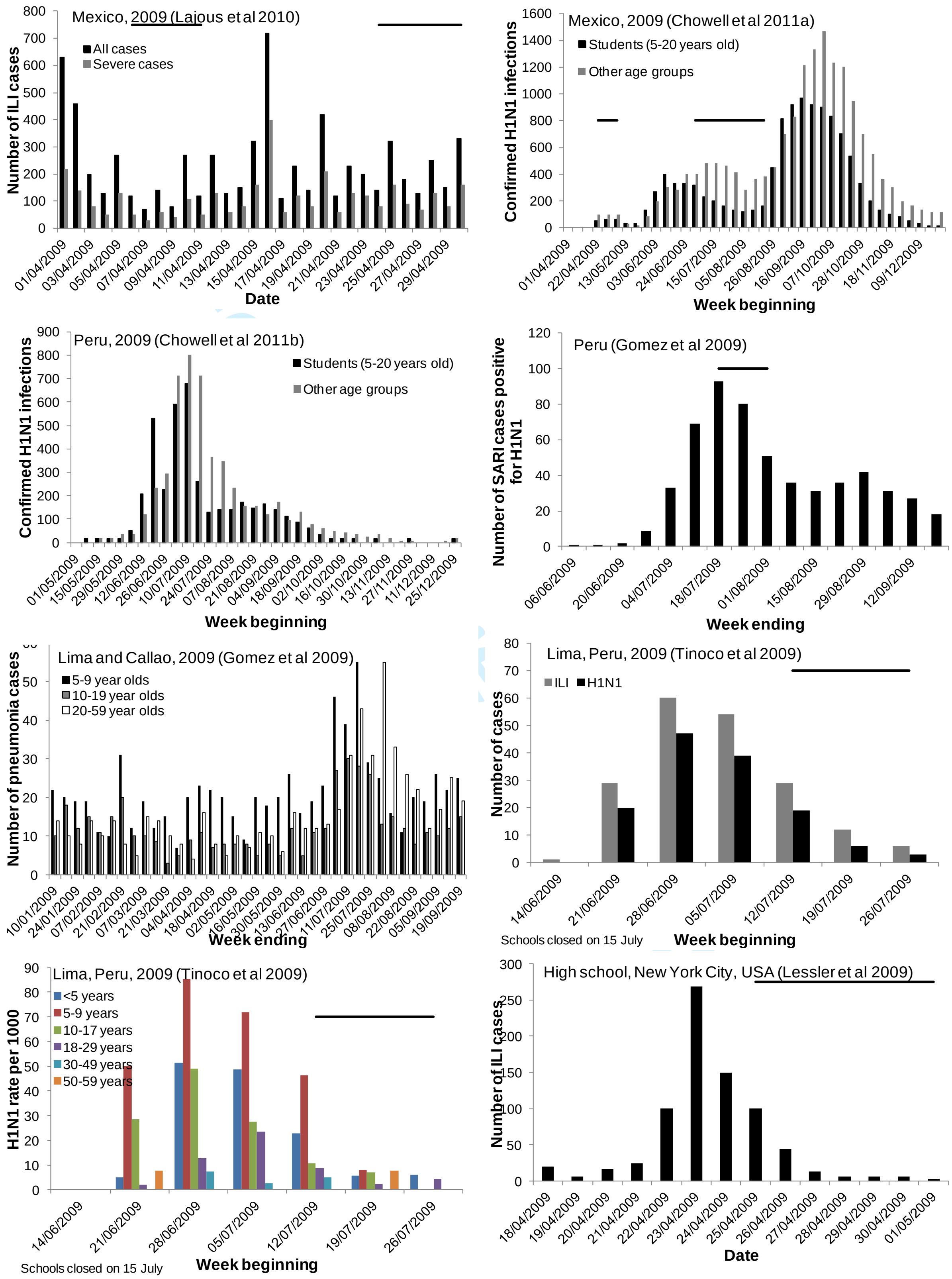

Yancey County, North Carolina, 2006
(Johnson et al 2008)
Number of clinical cases
Date

Supplementary Figure 2: Epidemic curves for pandemic influenza. Horizontal lines show periods of school closure (weekends are shown only if they are continuous with periods of pro-active or reactive closure). See Supplementary Table 2 for case definitions and full details of the datasets. School absenteeism data are denoted by an asterisk.

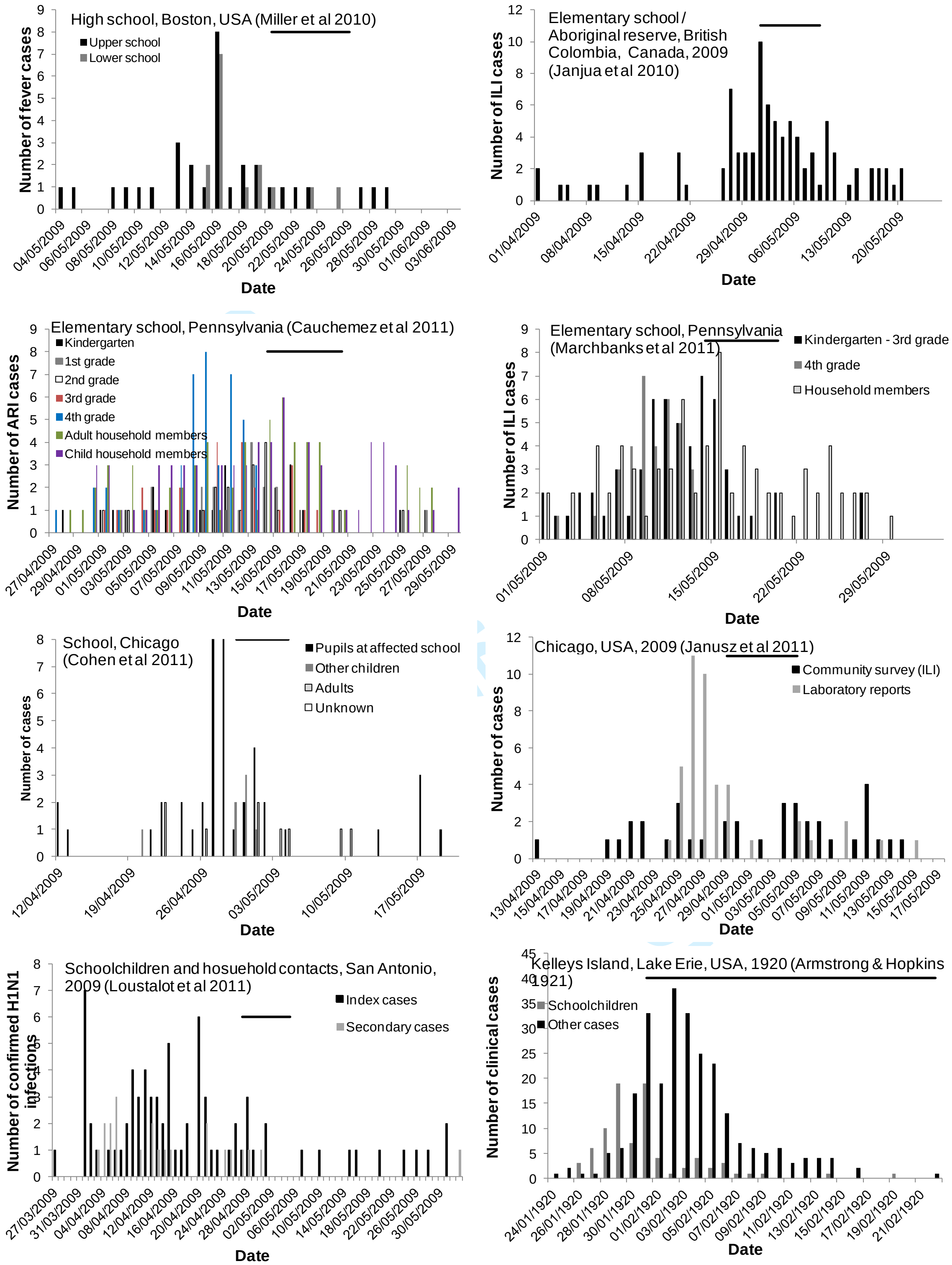


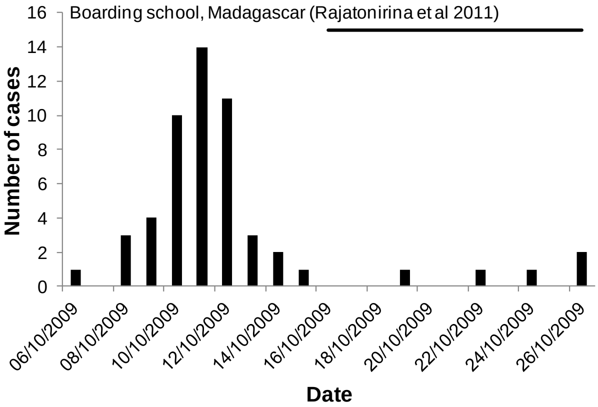

Secondary school, Toulouse, France (Guinard et al 2009)
Number of cases
Date
Includes both confirmed and probable cases
Paris, 2009 (Carrillo-Santisteve et al 2010)
Primary school
Nursery school
Families / friends
Number of cases
Date
Germany, 2009 (Poggensee et al 2010)
Practice index
Percentage of population with school holidays
Percentage of population living in states with school holidays
Week beginning
See Supplementary Information for definition of practice index
Vojvodina, Serbia 2009/10 (Petrovic et al 2011)
0-4 year olds
5-14 year olds
15-64 year olds
≥65 year olds
ILI consultation rate (per 100,000)
Week beginning
University and attached schools, Japan, 2009/10 (Uchida et al 2011)
Schoolchildren
University students
University staff
Number of cases
Week number (2009/10)
Japan (indigenously acquired cases only) (Nishiura et al 2009)
Number of confirmed cases
Date
Japan (Shimada et al 2009)
Number of confirmed cases
Date
Osaka, Japan (Kawaguchi et al 2009)
Number of confirmed cases
Date


Bangkok, 2009
(Chieochansin et al 2009)
All schools were closed for a public holiday 4-9/7/09 and in response to the outbreak 15-19/7/09. Tutorial schools were closed 13-28/7/09
Number of laboratroy confirmed H1N1 cases
Week beginning
Taipei City, Taiwan, 2009 (Hsueh et al 2010)
Hospitalisations
Class suspensions
Number of hospitalisations
Number of class suspensions
Week beginning
Primary school, Dongguan City, China, 2009 (Huai et al 2010)
Number of cases
Date
School, Hong Kong, 2009 (Leung et al 2011)
Schoolchildren
Household contacts
Number of confirmed H1N1 infections
Date
Israel, 2009 (Engelhard et al 2011)
<2 year olds
2-4 year olds
5-18 year olds
ILI consultation rate (per 10,000)
Week number (2009/10)
New Zealand, 2009 (Baker et al 2009)
ILI consultation rate (per 100,000 registered population)
Week ending
Three schools, Perth, Australia (Effler et al 2010)
One school closed completely, one cancelled classes for one grade, and one cancelled classes for three grades
Number of ILI cases
Date
Mexico (Echevarria-Zuno et al 2009)
Reporting requirements and case definition changed over the course of the outbreak. Schools closed in Mexico City and the State of Mexico on 24 April and nationally on 27 April. High schools reopened on 7 May and elementary schools on 11 May.
Some dates are taken from Stern & Markel 2009 or Cruz-Pacheco 2009.
Number of reported ILI cases
Date



Mexico, 2009 (Lajous et al 2010)
All cases
Severe cases
Number of ILI cases
Date
Mexico, 2009 (Chowell et al 2011a)
Students (5-20 years old)
Other age groups
Confirmed H1N1 infections
Week beginning
Peru, 2009 (Chowell et al 2011b)
Students (5-20 years old)
Other age groups
Confirmed H1N1 infections
Week beginning
Peru (Gomez et al 2009)
Number of SARI cases positive for H1N1
Week ending
Lima and Callao, 2009 (Gomez et al 2009)
5-9 year olds
10-19 year olds
20-59 year olds
Number of pneumonia cases
Week ending
Lima, Peru, 2009 (Tinoco et al 2009)
ILI
H1N1
Number of cases
Schools closed on 15 July
Week beginning
Lima, Peru, 2009 (Tinoco et al 2009)
<5 years
5-9 year years
10-17 years
18-29 years
30-49 years
50-59 years
H1N1 rate per 1000
Schools closed on 15 July
Week beginning
High school, New York City, USA (Lessler et al 2009)
Number of ILI cases
Date


High school, Boston, USA (Miller et al 2010)
Upper school
Lower school
Number of fever cases
Date
Elementary school / Aboriginal reserve, British Colombia, Canada, 2009 (Janjua et al 2010)
Number of ILI cases
Date
Elementary school, Pennsylvania (Cauchemez et al 2011)
Kindergarten
1st grade
2nd grade
3rd grade
4th grade
Adult household members
Child household members
Number of ARI cases
Date
Elementary school, Pennsylvania (Marchbanks et al 2011)
Kindergarten - 3rd grade
4th grade
Household members
Number of ILI cases
Date
School, Chicago (Cohen et al 2011)
Pupils at affected school
Other children
Adults
Unknown
Number of cases
Date
Chicago, USA, 2009 (Janusz et al 2011)
Community survey (ILI)
Laboratory reports
Number of cases
Date
Schoolchildren and hosuehold contacts, San Antonio, 2009 (Loustalot et al 2011)
Index cases
Secondary cases
Number of confirmed H1N1 infections
Date
Kelleys Island, Lake Erie, USA, 1920 (Armstrong & Hopkins 1921)
Schoolchildren
Other cases
Number of clinical cases
Date


Boarding school, Madagascar (Rajatonirina et al 2011)
Number of cases
Date
0
2
4
6
8
10
12
14
16
06/10/2009
08/10/2009
10/10/2009
12/10/2009
14/10/2009
16/10/2009
18/10/2009
20/10/2009
22/10/2009
24/10/2009
26/10/2009

## Supplementary Table 1: Studies of the effects of school closures on seasonal influenza outbreaks

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| **Europe** | | | | | | | |
| Briscoe (1977) [1] | Outbreak report / estimate of vaccine efficacy | 1231 boys at Eton College, 1976 (79% of whom were vaccinated). Age of pupils not stated but the school currently takes boys aged 13-18. | Planned half term holiday | Friday 20 to Monday 23 February | Epidemic began in late January, first wave peaked 6 February, second wave peaked 17 February. | Clinical influenza (n = 372); confirmed as influenza A in 6/8 swabbed cases and influenza B in 1/8. | One case on day before break, ~12 cases on following day. ~1-4 cases/day for rest of study period. Hypothesised that closure curtailed the epidemics in individual school houses. 15/26 houses had no further cases after the break. |
| Davies et al (1988) [2] | Non-controlled intervention study of prophylactic amantadine | 859 boys aged 11-18 years at Christ's Hospital boarding school, 1986 | Planned half term holiday | Friday 21 to Monday 24 February | Epidemic began in early February, prophylaxis began on 5 February coinciding with the peak | Clinical influenza (n = 181); confirmed as influenza A H3N2 in majority of cases | 0-3 cases/day in five days preceding closure; 12 cases over 4-day closure period. Daily case numbers immediately following re-opening similar to those before closure. |
| Grilli et al (1989) [3] | Outbreak report | 675 boys aged 11-18 years at Christ's Hospital boarding school, 1985 | Planned mid-term break | 22-24 February | Epidemic began in late January and appeared to peak (at ~19 cases) 4 days before closure | ILI in pupils reporting to school infirmary (n = 206), the majority of which were confirmed as influenza. | 4-5 cases on each of the 2 days before closure; 15 cases occurred during closure (no daily breakdown is provided). ~0-6 cases occurred per day over the month following reopening. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Danis et al (2004) [4] | Outbreak report | 802 pupils at boys' secondary school (age 11-18 years), Ireland, 2003 | Response to outbreak | Whole school closed 4-11 September; 6th class sent home earlier (date not stated) | Whole school closure from day after peak of outbreak | ILI in absentees ascertained through telephone and questionnaire surveys (n = 107); confirmed as influenza in 12/15 cases | Peak incidence ~45 cases on day before closure; 18 cases on first day of closure and continuing decline thereafter. Only 2 cases after re-opening (although there was no active case finding at this point). Little evidence of community spread after the school outbreak. |
| Miller and Lee (1969) [5] | Outbreak report | England and Scotland (all ages), November 1967 – February 1968 | Planned Christmas holiday | Two weeks, all schools | Schools closed during the growth phase of the epidemic in most age groups | Age-specific rates of influenza reported by general practitioners | Rates in 0-4, 15-44, 45-64 and ≥65 year olds peaked during the second week of closure, rates in 5-14 year olds were in decline at this point. Following reopening, increases occurred in the 0-4 and especially 5-14 year age groups. |
| Cauchemez et al (2008) [6] | Statistical / transmission modelling analysis based on fitting to surveillance data | French national sentinel surveillance system, 1985-2006 (covering all ages, over 60 epidemic periods and from ~1% of practicing GPs) | Routine school holidays | Approx 2 weeks in each of December – January, February – March, March-April. Timing varies by 1-2 weeks in the 2-3 holiday zones. | Varied between epidemics | Rates of influenza-like illness reported through sentinel GPs | Estimated that holidays resulted in a 20-29% (median 24%) decrease in rate of transmission to children, without affecting contacts made by adults; this translated to a reduction in the attack rate of 16-18% overall (14-17% for adults, 18-21% for children) |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| **Asia** | | | | | | | |
| Olson et al (1980) [7] | Outbreak report | Grades 1-6 (2831 students) of Girls Teachers' Colleges Primary School, Taipei and grades 1-6 (650 students) of Taipei American School , Taiwan, September 1975 – May 1976. Ages of students not stated. | Planned holiday during virologically confirmed community influenza outbreak | Six weeks (Girls Teachers' Colleges Primary School); 3 weeks (Taipei American School) | Relationship with influenza circulation unclear, but likely to be late in the outbreak. Absenteeism at Girls Teachers' Colleges Primary School peaked two weeks before closure; absenteeism at Taipei American School had not exceeded the epidemic threshold at the time of closure. | School absenteeism (all cause) | Girls Teachers' Colleges Primary School: absenteeism declined from ~1.65 absences per child-day in the week before closure to ~0.7 absences per child-day (only slightly above expected absenteeism of 0.65) in the week following re-opening. Taipei American School: absenteeism very similar before and after closure |
| Sonoguchi et al (1985) [8] | Cohort study of the extent of cross-protection between influenza subtypes | 173 children (of 245 enrolled) aged 13-14 at a middle school in Tokyo; 347 children (of 374 enrolled) at a high school in Kumamoto prefecture, Japan. >90% vaccination coverage at each school. | Planned winter holiday (middle school); response to high levels of absenteeism (high school) | Two weeks (middle school); 3 days (high school) | Middle school: case numbers were fairly constant at <5/day during the week before closure. High school: epidemic appeared to be in decline when school closed but case numbers increased on reopening. | Absenteeism while the schools were open; serious, confirmed influenza A infection during closure periods. | Middle school: case numbers remained low at 0-2 per day during closure. High school: case numbers declined from 16 on the day before closure to 13, 5 and 0 on the three days of closure, rebounding to 21 on the day of reopening. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Fujii et al (2002) [9] | Presentation of surveillance data | Children aged 4-14 years attending 36 sentinel surveillance in Japan, 1999-2000 | Planned holiday | 2 weeks | Case numbers began to increase from week 50 of 1999; schools closed week 52 and week 1. | Medically attended clinical ILI | 191 cases in week before closure, declining by 38% to 118 cases during the first week of closure. Incidence increased to 173 cases during the second week of closure and an epidemic followed when schools reopened. |
| Heymann et al (2004) [10] | Ecological before-and-after comparison | All 6-12 year old children (n = 186094) registered with one of the four national healthcare insurance schemes, Israel, 2000 | National teachers' strike affecting ~80% of 6-12 year old children [11] coinciding with influenza outbreak | 2 weeks (16-28 January 2000), elementary schools nationwide. Ultra-orthodox schools, preschools and high schools remained open. | Outbreak began in last week of December 1999; schools closed 16-28 January 2000. | Medically attended / diagnosed respiratory tract infections (MARI); All physician visits; All outpatient clinic visits; All emergency department visits; hospitalisations; medication purchases (antibiotics, antipyretics, cold and cough medicines). | MARI: number of cases decreased by 42% and 27% during closure period and following fortnight respectively, compared to the fortnight before the closure.* Physician visits: rate ratios 0.78 and 0.88* No effect on hospital admissions. |
| Lo et al (2005) [12] | Ecological before-and-after comparison | Respiratory specimens (all ages) processed by Government Virus Unit, Hong Kong, 1998-2003 | Reaction to SARS outbreaks; other social distancing and hygiene measure also implemented | Not stated, but general community control measures were in effect at least in April – June 2003 | Not clear | Proportion of respiratory specimens positive for influenza | Monthly proportions positive were 58-88% lower in April – June 2003 than the average for the corresponding months of 1998-2003, but the difference with specific years was variable (e.g. little difference with the low influenza years of 1999 and 2000). |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Cowling et al (2008) [13] | Ecological before-and-after comparison with modelling analysis | Hong Kong population (all ages), 2008 | Reactive closure for 1 week in response to 3 influenza deaths in children, followed by scheduled 1 week Easter break. | 2 weeks (including Easter break) – all primary schools, special schools, kindergartens and day nurseries. | Outbreak began in January and peaked in February; schools closed 13 March. | Influenza A and B isolations from surveillance data as proportion of all specimens (for children and adults separately); sentinel ILI consultation rates; influenza hospital admission rates in children aged <5 years; estimates of effective reproduction number. | Continued decrease in already declining incidence measures; no apparent meaningful change in effective reproduction number. |
| Heymann et al (2009) [11] | Ecological before-and-after comparison, with comparison to years not affected by atypical school closure | Individuals aged ≥6 years registered with a specific healthcare service provider in Israel, 1998-2002 | Teachers' strike affecting ~80% of children, coinciding with influenza outbreak in 2000; Hanukah holidays in all years. | 8 days each year for Hanukah holiday; 2 week closure (16-28 January 2000) of elementary schools nationwide, excluding ultra-orthodox, preschools and high schools. | Closure due to strike as Heymann (2004) [10]; timing of Hanukah holidays in relation to respective epidemics not clear. | Ratio of number of clinic visits for ILI to number for non-respiratory illness, in 6-12 year olds and individuals aged over 12 (calculated separately for those living with and without 6-12 year olds). | Decrease in ratio of 15% for 6-12 year olds associated with the strike; decreases in adults were not statistically significant. In some years, there was evidence of a reduction in the ratio for adults and/or children associated with the Hanukah holidays. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| **Australasia** | | | | | | | |
| Cashman et al (2007) [14] | Outbreak report | Secondary boarding / day school (age of pupils not stated), New South Wales, Australia, August 2006 | Planned closure coinciding with outbreak of ILI and pneumonia | Four days | Unclear, but closure appears to have occurred late in outbreak | Presentations to sick bay with respiratory illness (n not stated). Influenza A H3N2 isolated from 5 students | Respiratory presentations decreased following closure, returning to baseline within 7 days (no further quantitative information provided). |
| Shaw et al (2006) [15] | Outbreak report | Single school in Wellington, New Zealand, May-June 2005 – 350 pupils in years 1-8. | One closure in response to high levels of absenteeism; later closure for a “holiday weekend” | Two closures of 4 days each, including weekends in both cases | Peak absenteeism occurred on the day before the first closure; epidemic was generally declining before the second closure | School absenteeism (all causes) | For both closures, absenteeism was lower on reopening than before the closure. |
| **Americas** | | | | | | | |
| Leonida (1970) [16] | Outbreak report | Five elementary schools (student population 2314) and three high schools (student population 8012) in Skokie, Illinois, September 1967 – April 1968 | Winter holiday | One week at the end of November and two weeks at the end of December; all schools in the sample | First closure 2 weeks before peak in elementary schools and 2 weeks after peak in high schools; second closure 2 weeks after peak in elementary schools and 6 weeks after peak in high schools. | School absenteeism due to ILI. | First closure had no clear effect on the increase in absenteeism at the elementary schools or the decline in the high schools. Absenteeism continued to decline in both elementary and high schools during the second closure; no apparent increase on reopening. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Glass et al (1978) [17] | Outbreak report | Mercer County, New Jersey, USA, November 1977 – March 1978 | Planned Christmas holiday | One week (public schools) or two weeks (residential schools) | Around peak of outbreak | Absenteeism from 6 public schools, work absenteeism, febrile illnesses in nursing homes, admissions to three residential school infirmaries, emergency room visits, hospital admissions for acute respiratory disease, P&I deaths, viral isolates | School absenteeism was lower after the holiday than before and gradually increased, reaching a plateau at a level slightly higher than before the closure. Emergency room visits and hospital admissions peaked during the closure week and viral isolates the week before. |
| Farley et al (1992) [18] | Outbreak report / estimate of vaccine efficacy | Boarding school, Connecticut (989 pupils in grades 9-12), January – April 1989 | Planned holiday | Three weeks | Epidemic appeared to be largely over by the time of the holiday (there were ~8 cases in the week before closure; the peak had occurred 5 weeks previously) | Admission to school infirmary with fever or respiratory symptoms ( n ~135) | Number of admissions remained low (≤8 per week) after reopening. |
| Louie et al (2007) [19] | Description of several surveillance systems during one influenza season | California, week 40 of 2005 to week 15 of 2006 | Planned winter holiday | Two weeks; presumably all schools | ILI peaked week before closure; laboratory isolations appeared to be increasing when schools were closed. | ILI reported through sentinel surveillance system (expressed as the proportion of all visits that were for ILI); number of laboratory-confirmed influenza from sentinel laboratories. | ILI declined throughout school closure and remained at low levels following reopening; laboratory-confirmed infections declined slightly in the first week of closure, then increased before declining after schools reopened. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Johnson et al (2008) [20] | Outbreak report focussing on effects of closure on families | 355 children enrolled in all 9 public elementary, middle and high schools in Yancey County, North Carolina, USA, 2006. | Closure for operational reasons, due to high levels of staff absenteeism largely attributed to ILI. | 10 days (2 – 12 November) - all 9 schools in the county. | First reported onset (in study sample) 20 October, epidemic peak 1 November, schools closed 2 November. | Parentally-reported ILI (n = 123) ascertained through telephone survey | Incidence decreased from peak of 8 cases the day before closure to 5 cases on the first day of closure, and continued to decline thereafter. |
| Rodriguez et al (2009) [21] | Cohort study comparing schools which cancelled their winter break to those which did not | 265 elementary, middle, high and "other" schools which closed and 205 which did not, King County, Washington, February – March 2007 | Planned holiday closure coinciding with influenza outbreak | 1 week, including middle, high and other public and private schools | Closure immediately following epidemic peak | School absenteeism (all causes) | No evidence of a difference in absenteeism following the break between schools that closed and those that did not. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Wheeler et al (2010) [22] | Ecological before-and-after comparison covering fortnights before, during and after school closure in 4 influenza seasons. | General population of Arizona, 2004/05 – 2007/08 influenza seasons. | Planned winter holidays | 2 weeks, all schools in the state | Peak occurred at least 2 weeks after reopening in 3 of the 4 seasons; peak coincided with the second week of closure in the remaining season. | Influenza laboratory reports 2004/05 to 2007/08 (n = 833 in school-aged children, 4036 in other age groups); influenza hospitalisations 2004/05 to 2006/07 (n = 885 in school-aged children, 4512 in other age groups). | For school-aged children, incidence never significantly increased during the two weeks of closure compared to the preceding two weeks; incidence in the two weeks following reopening either increased (2 seasons), declined (1 season) or was unchanged compared to the weeks of closure.<br>For other age groups, incidence consistently increased during the closure period; changes on reopening were inconsistent. |

* Recalculated from data provided in paper

## Supplementary Table 2: Studies of the effects of school closures on pandemic influenza

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| **Europe** | | | | | | | |
| Smith et al (2009) [23] | Outbreak report | 1307 pupils aged 13-18 at a boarding school in SE England, May – June 2009 | Scheduled break extended in response to outbreak; prophylactic oseltamivir also used | 11 days (4 day scheduled break extended by 7 days). Some pupils returned ~1 week earlier for exams | Closed around time of epidemic peak | Clinical ILI in pupils attending school healthcare facilities 1-27 May; laboratory-confirmed H1N1v after 27 May (n = 102 including both clinical and confirmed cases) | Apparent decline in cases in pupils following closure; no information on other age groups |
| HPA West Midlands H1N1v Investigation Team (2009) [24] | Outbreak report | 479 primary and nursery school pupils (aged 4-12), plus 84 staff, at a school in Birmingham, England, May 2009 | Scheduled break extended in response to outbreak; prophylactic oseltamivir also used | 11 days (9 day scheduled break extended by 2 days) | After epidemic peak | Laboratory confirmed H1N1v (n = 64) | Case numbers in pupils and staff declined following closure (e.g. from 8 cases on the day of closure to 5 on each of the two following days). No further cases following re-opening. Limited information on illness in other groups. |
| Wallensten et al (2009) [25] | Outbreak report | 248 Year 7 pupils at a school in SW England (93% of the year group, aged 11-12 years), April – May 2009 | Response to outbreak; prophylactic oseltamivir also used | 10 days | Unclear | Prevalence of self-reported ILI during the week before closure, the closure week, and the following week | 5, 11 and 10 children had symptoms compatible with the case definition in the week before, during and after closure, respectively. Absenteeism was almost identical in the weeks before and after closure. No information on illness in other age groups. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Calatayud et al (2010) [26] | Outbreak report | 1177 pupils (year groups Reception to 13), plus staff, at a school in London, May 2009 | Response to outbreak (preceded by closure for Easter several weeks previously); use of prophylactic oseltamivir | 3 days of Easter holiday remained after onset of first possible case; reactive closure lasted 9 days (including 2 weekends). | One possible case occurred 3 days before the end of the Easter closure and did not attend school while symptomatic; no further cases occurred until the main outbreak began ~7-10 days after this possible case. Reactive closure occurred the day following the peak (6 cases). | Virologically confirmed or possible (symptomatic without combined nose and throat swab but pending serological results) H1N1 infection | Cases continued to occur at 3-4 cases / day for 4 days following reactive closure. On the 5th and 6th days, there were 0 and 1 cases, respectively, and no cases subsequent to this. |
| Strong et al (2010) [27] | Outbreak report, focussing on use of antivirals | 297 pupils (aged 7-12 years) and 58 staff at a primary school in Sheffield, June 2009 | Response to outbreak; oseltamivir used for treatment and prophylaxis | One week | Epidemic peaked 3 days before closure. | Self-reported ILI (n = 61) | Incidence continued to decline while school was closed; no data presented for period after reopening. |
| Baguelin et al (2010) [28] | Modelling study of cost-effectiveness of vaccination; includes incidence data spanning term time and holiday periods. | England & Wales population, June – October 2009. | Planned summer holiday. | ~ 6 weeks, all schools nationally. | Closure coincided with peak of the first wave. | Health Protection Agency estimates of numbers of infections, rescaled (multiplied by 10) to reflect under-reporting. | Incidence declined throughout the period of school closure and increased after schools reopened, producing a second wave of infection. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Guinard et al (2009) [29] | Outbreak report | 30 students (aged 11-12 years) and 18 staff from one affected class, at a secondary school in Toulouse, France, June 2009 | Reactive closure in response to outbreak; some use of prophylactic oseltamivir | 7 days | At apparent end of epidemic | Probable H1N1v infection with or without laboratory confirmation (n = 17 with known date of onset, plus 3 without) | No further cases in pupils or their contacts following closure, but epidemic appeared to be over before the school was closed. |
| Carrillo-Santisteve et al (2010) [30] | Outbreak report | Two primary schools (360 and 293 aged 6-11 years), a nursery school (253 children aged 3-6 years) and a daycare school (unknown number of children aged 3 months to 3 years), Paris, June 2009; the four schools shared some facilities. | Response to outbreak which began in one of the primary schools; close contacts were given prophylactic oseltamivir. | 9 days (including 2 weekends), one of the primary schools and the nursery school (these schools accounted for 59/66 cases in pupils) | Officially closed on day of peak, but weekend began two days previously. | Confirmed and probable influenza cases in children attending the closed schools and their families and friends who consulted influenza outpatient clinic (n = 81) | Incidence in the closed primary school peaked on the 3rd day of closure (12 cases) and fell to 2 cases on each of the two following days; no further cases occurred. Incidence in the closed nursery school increased through the first 3 days of closure to a peak of 6 cases, then declined to 0-1 cases per day for 4 days; no further cases occurred after this. Cases in families and friends of the schoolchildren (n = 15) occurred only during the period of school closures. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Poggensee et al (2010) [31] | Outbreak report | General population of Germany, April – November 2009 | Planned holiday. | Duration not stated; school closure is described using the weekly "vacation density" (the percentage of the population living in states in which schools were closed) as the timing of the holiday varied between states | Vacation density peaked in the early stages of the outbreak, while the practice index was below the seasonal threshold and not increasing markedly. A second increase in the vacation density occurred while the practice index was increasing linearly. | Acute respiratory illness reported through sentinel surveillance system, used to calculate a "practice index" (defined as "the relative deviation of observed consultations for ARI divided by all consultations in the same week and set into relation to the background value of this ratio in weeks without influenza virus circulation") | Practice index remained fairly constant throughout the main school holiday period and increased only when the vacation density was declining; the second increase in the vacation density was followed by a brief plateau in the practice index. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Birrell et al (2011) [32] | Modelling analysis | General population of London, UK, May – December 2009 | Planned holidays | Six week summer holiday and two half terms of one week each (in May and October); all schools in London closed. | As Baguelin et al [28] (closure coincided with peak of the first wave) | Influenza-like illness recorded through GP sentinel surveillance scheme together with serological and virological data; parameters estimated included the reduction in contact rates associated with school holidays. | Both peaks in the two waves of consultations coincided with a school holiday. The summer holiday was estimated to reduce contacts amongst 5-14 year olds by 72% and the half term holiday by 48%; no effects were apparent in other age groups. |
| Evans et al (2011) [33] | Estimation of numbers of ILI cases due to pandemic H1N1 based on GP consultation data, helpline usage, virological swabbing and assumptions about the proportion of infections resulting in healthcare seeking. | General population of England, June – December 2009. | Planned holiday. | Six week summer holiday affecting all schools nationally. | As Baguelin et al [28] (closure coincided with peak of the first wave) | Estimate numbers of ILI cases due to pandemic H1N1, by age and region. | Estimated incidence declined during the school holiday and increased following reopening, in all regions and in all age groups except for the <1 and ≥65 year olds (among whom estimated case numbers were low). |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Smith et al (2011) [34] | Analysis of telephone helpline (NHS Direct) and GP consultation data | General UK population, May – August 2009; results also presented separately for London and West Midlands regions. | Planned school summer holiday (late July to early September). | Approximately six weeks; all schools nationally. | First week of school closure coincided with national peak in NHS Direct calls but occurred after the peak for London and the West Midlands. Consultation data peaked in the first week of closure nationally and before closure in London. | Weekly percentage of calls to NHS Direct that were classified as cold / flu. Weekly GP consultation rates for ILI. | Both indices continued to decline during closure; no data presented after schools reopened. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Flasche et al (2011) [35] | Statistical analysis of relationship between estimated effective reproduction number for H1N1 pandemic influenza in 12 European countries (in 2009) and several explanatory variables, including school holiday dates | General populations in Belgium, Bulgaria, England, France, Germany, Italy, Luxembourg, Netherlands, Portugal, Romania, Slovakia and Spain, April – October 2009. School holidays occurred during the study period in all countries except Bulgaria, England and France. | Planned holidays. | Varied by country. | Varied by country, but typically early in the respective outbreaks. | Effective reproduction number estimated from numbers of laboratory-confirmed pandemic H1N1 infections. | No evidence found of a relationship between the effective reproduction number and the start of school holidays. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| van Gageldonk-Lafeber et al (2011) [36] | Outbreak report; comparison of pandemic and seasonal ILI consultation data. | General population of the Netherlands, and residents of nursing homes considered separately, October – December 2009 | Planned holidays | One week; all schools nationally although timing varied by region. | In north and central regions, schools closed two weeks after the epidemic threshold consultation rate was exceeded nationally; in the south, schools closed one week later. | GP consultation rates for ILI (age-stratified); ILI rates in nursing home residents; age-specific H1N1 hospital admission rates. | Possible reduction in incidence, or slowing of epidemic growth, among 0-4, 5-9, 10-14 and 15-19 year olds; epidemic continued to grow after schools reopened. No apparent effect of school closure on ILI in nursing home residents or hospital admissions. |
| Merler et al (2011) [37] | Modelling analysis of factors influencing spatiotemporal spread of pandemic H1N1 in Europe | General population of 37 European countries, May – December 2009 | Mainly planned holidays; some reactive closures. | Varied by country; summer holidays typically lasted 6-12 weeks and autumn holidays approximately 2 days to 2 weeks. | Varied by country. | Predicted numbers of infections for comparison with ILI surveillance data. | The model reproduced the observed incidence patterns in the different countries most closely when country-specific school holidays were included and contact rates in the population were allowed to change during holidays. (Transmission was assumed to be eliminated in schools and increased by a factor of 1.4 in the community during holidays.) |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Petrovic et al (2011) [38] | Outbreak report / analysis of risk factors for death in hospitalised cases. | Catchment population (n = 102,723) of general practices participating in sentinel surveillance, Vojvodina, Serbia, September 2009 – April 2010. | Response to outbreak. | All schools in Vojvodina; a closure lasting one week was followed six weeks later by a three week closure. | First closure coincided with first peak in ILI consultations in all ages and 5-14 year olds, but after the peak in 0-4 year olds. Second closure occurred after peak. | ILI consultation rates, overall and by age group. | ILI consultation rates declined following first closure and increased after schools reopened, particularly in 5-14 and 15-64 year olds. Rates were already declining when schools closed for second time and continued to do so during closure; possible slight increase after reopening. |
| **Asia** | | | | | | | |
| WHO (2009) [39] | Outbreak report, primarily reporting clinical aspects of infection | School pupils in Hyogo Prefecture and Osaka Prefecture, Japan, May 2009 | Response to school-associated outbreak | 7 days, >1400 schools closed but unclear whether this represents all schools in the two prefectures | Unclear | School absenteeism | No increase in school absenteeism upon reopening of schools (no quantification of absence levels given) |
| Nishiura et al (2009) [40], Shimada et al (2009) [41] | Outbreak reports (both report essentially the same data with slightly different analyses) | General Japanese population, May – June 2009 | Response to outbreak associated primarily with schools; some use of prophylactic oseltamivir [39] | 7 days (possibly more in some cases), all schools in Hyogo and Osaka prefectures (preceded by weekend closure) | First confirmed cases had disease onset on 9 May, weekend / closure began 16 May | Laboratory-confirmed H1N1 influenza (restricted to indigenously-acquired cases in [40] (n = 361[40] or 392 [41]) | Case numbers peaked at ~70 cases on the second day of the weekend, then declined throughout week of closure; no obvious resurgence on reopening |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Kawaguchi et al (2009) [42] | Outbreak report (subset of the data used in the two studies above) | Schools in Osaka Prefecture, Japan, May 2009; ages of affected students not stated. | Response to outbreak; some use of prophylactic oseltamivir in families of cases | 1 week (preceded by a weekend), all 270 high schools and 526 junior high schools, and most nurseries, primary schools, colleges and universities, in Osaka prefecture | Epidemic peaked on second day of closure (i.e. at the weekend) | Confirmed H1N1 infection (n = 156) | Peak of 30 cases on second day of weekend and declined throughout closure period; no resurgence after re-opening |
| Chieochansin et al (2009) [43] | Outbreak report | General population of Bangkok, June – July 2009 | Public holiday followed later by closure in response to outbreak | Public holiday lasted 1 week; schools were subsequently closed for 1 week and tutorial schools for 2 weeks | Public holiday occurred during peak week. Closure of schools and tutorial schools began during the following week. | Laboratory confirmed pandemic H1N1 influenza | Incidence declined throughout period of closure. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Wu et al (2010) [44] | Age-structured SIR model fitted to data on laboratory-confirmed cases during the 2009 pandemic in Hong Kong, used to estimate reporting rates and the reduction in within age group transmission resulting from school closures | General population of Hong Kong, June – August 2009 | Response to outbreak, followed by planned school holiday | All primary schools, kindergartens, childcare centres and special schools closed for ~1 month immediately prior to the summer holiday (duration of holiday not stated). Secondary schools with ≥1 case closed for 14 days, all secondary schools closed for summer holiday at same time as primary schools | At start of growth phase of first wave, which peaked around the 10$^{th}$ day of closure. School holidays started at the beginning of the growth phase of a second wave. | Laboratory-confirmed pandemic influenza cases, proportion of these in different age groups (0-12 years, 13-17 years and ≥18 years) and percentage reduction in within age group transmission resulting from school closures. | First wave continued to grow during school closure, followed by second wave beginning around the start of the school holidays. Following school closure, numbers of cases in 0-12 year olds remained low but the proportion of cases in this age group increased slightly, while that in 13-17 year olds decreased. School closure was estimated to reduce transmission between children of the relevant age group by 70% (95% CI 64-75%), corresponding to an overall reduction in transmission of ~25%. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Cowling et al (2010) [45] | Modelling analysis | General population of Hong Kong, May – October 2009 | Response to outbreak, followed by planned school holiday | All primary schools, kindergartens, childcare centres and special schools closed for ~1 month immediately prior to the summer holiday (duration of holiday not stated). Secondary schools with ≥1 case closed for 14 days, all secondary schools closed for summer holiday at same time as primary schools | At start of growth phase of first wave, which peaked around the 10th day of closure. School holidays started at the beginning of the growth phase of a second wave. | Laboratory-confirmed pandemic influenza cases and hospitalisations, used to estimate daily values of the effective reproduction number. | Effective reproduction number declined during initial days of closure, oscillated around 1 for the duration of the closure period, increased very slightly when schools reopened before declining again. |
| Hsueh et al (2010) [46] | Outbreak report | General population of Taipei City, Taiwan, June 2009 – January 2010 | Response to outbreak | Individual classes suspended for at least 5 days if >2 students had confirmed infection within 3 days. | Timing for individual schools not presented; number of class suspensions generally increased with the number of hospitalisations. | Hospitalisations with pandemic H1N1. | Number of class suspensions generally followed the number of hospitalisations. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Wu et al (2010) [47] | Vaccine study amongst children attending public primary and middle schools and participating in a national celebration parade. | 95244 vaccinated participants in a national celebration parade, Beijing; of these, 25037 vaccinated schoolchildren were compared to 244091 unvaccinated schoolchildren. | Planned national holiday | 1 week, all schools nationally. | Schools closed as cumulative incidence in unvaccinated students began to plateau | Laboratory confirmed H1N1 infection | Cumulative incidence in unvaccinated children increased very slightly during the school closure (from ~220 to ~260 per 100,000); rate of increase in cumulative incidence increased ~1 week after schools reopened. Cumulative incidence in vaccinated students remained relatively constant before, during and after school closure. |
| Huai et al (2010) [48] | Outbreak report | Primary school (1314 pupils) in Dongguan City, Guangdong Province, China, June 2009 | Response to outbreak, shortly followed by planned summer break. | Affected primary school closed 19-28 June; all schools in the town closed 22-28 June, Planned summer break began on 2 July. | Affected school closed on day of peak. | Confirmed or suspected cases in children attending affected school (n = 105); limited data on cases in the community are also included. | Epidemic in schoolchildren peaked at 30 cases on the first day of closure, declining to 11 the following day. No further cases occurred between the last two days of closure and the subsequent closure for the holiday. |
| Engelhard et al (2011) [49] | Outbreak report | Children aged <18 years enrolled with one health maintenance organisation in Israel, June 2009 – April 2010. | Two separate planned holidays. | Summer holiday lasted 9 weeks, autumn holiday lasted 5 weeks. | Summer holiday occurred close to beginning of first wave; autumn holiday close to beginning of second. | Rate of ILI (fever with one or more of cough, coryza, sore throat, myalgia) visits to community health clinics. | ILI rate peaked and decliend during summer holiday, began to increase when schools reopened and reached a second peak during the autumn holiday before declining again. A third wave occurred after the autumn holiday. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Leung et al (2011) [50] | Outbreak report / analysis of household secondary attack rates and effect of oseltamivir. | 511 children attending a secondary school in Hong Kong and their 205 household contacts, June 2009. No cases occurred amongst the 153 school staff. | Response to outbreak | Two weeks, coinciding with closure of all schools in Hong Kong. | Three days after peak. | Laboratory-confirmed pandemic H1N1 in schoolchildren or household contacts. | Incidence increased during first two days of closure and subsequently remained very low; last case occurred one week before reopening. |
| Uchida et al (2011) [51] | Prospective study of pandemic H1N1 | 2318 schoolchildren, 11424 university students and 3344 staff members associated with Shinshu University Organisation, August 2009 – March 2010 | Planned breaks and reactive closures. | Planned summer holiday affected all schools for approximately one month; winter holiday for 3 weeks; reactive school and class closures varied for individual schools. | Summer holiday occurred before outbreak began; winter holiday occurred while incidence was declining. Timing of reactive closures in relation to incidence in individual schools unclear. | "Influenza-like symptoms and diagnosed with confirmed, probable or suspected swine flu at hospital or clinics." | Incidence continued to decline during the winter holiday. Incidence also appeared to declined during reactive school and class closures, but this is unclear as data are not presented for individual schools. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| **Africa** | | | | | | | |
| Rajatonirina et al (2011) [52] | Outbreak report / analysis of oseltamivir compliance and side effects. | 132 boarders at a school in Antananarivo, Madagascar, October – November 2009. | Planned holiday | 2 weeks | After main phase of epidemic. | At least one influenza-like symptom (n = 56 with known onset date). | Epidemic appeared to be largely over when the school closed; sporadic cases continued to occur during closure period. |
| **Australasia** | | | | | | | |
| Caley et al (2008) [53] | Transmission modelling analysis of hospitalisation and mortality data | Sydney, 1919 (all ages) | Response to outbreak; combined with other social distancing interventions | ~4.5 weeks initially; schools reopened for ~3 weeks and then closed for a further ~2 months. | Initial closure occurred as first cases were detected; second closure occurred during exponential growth phase of epidemic. | Estimated reduction in “behaviours resulting in disease transmission.” | Transmission reduced by 38% during period of school closure. |
| Baker et al (2009) [54] | Outbreak report | New Zealand population, April – August 2009 (all ages) | Planned national holiday during national outbreak; some use of prophylactic antivirals during containment phase [55] | 2 weeks, apparently all schools nationally | Depending on indicator, closure coincided with peak, preceded it by 1 week, or followed it by 1-3 weeks | Cases reported through notifiable disease surveillance system (n = 3179); hospitalisations amongst these cases (n = 972); ICU influenza admissions (n = 106); GP consultation rates (two surveillance systems) | Notifications, hospitalisations and ICU admissions began to decline during second week of closure. GP consultation rates for 5-14 year olds increased following re-opening (in one of the systems only). |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Effler et al (2010) [56] | Outbreak report focussing on children's activities during closure and the effects of closure on families | Three schools in Perth, Western Australia, May – July 2009; ages of affected pupils not stated. Data available for 233 of 402 students. | Response to outbreak | 1 week; one school closed completely and two closed only affected year groups | Confirmed cases in individuals attending the three schools peaked two days before closure | Confirmed pandemic H1N1 infection | Confirmed cases peaked at ~9/day two days before closure, subsequently a maximum of 1 case / day occurred. |
| Paine et al (2010) [57] | Outbreak report and modelling analysis | New Zealand population, April – November 2009 (all ages) | Planned national holiday during national outbreak; some use of prophylactic antivirals during containment phase [55] | 2 weeks, all schools nationally | ~4 days before peak. | Cases reported through notifiable disease surveillance system (n = 3254), used to estimate daily values of the effective reproduction number | Case numbers peaked and declined during holiday, no consistent increase when schools reopened. Effective reproduction number was declining before school closure and continued to decrease during the holiday, appeared to increase slightly and reach a plateau after schools reopened. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| **Americas** | | | | | | | |
| Cruz-Pacheco et al (2009) [58] | Estimation of contact rates based on estimated values of $R_0$ before and after introduction of control measures | Mexico City, April – May 2009 (all ages) | Response to outbreak; no use of antivirals | ~2.5 weeks, all schools in Mexico City. | Epidemic had been growing exponentially for ~1 week when schools were closed | Number of confirmed (n = 1752) or probable (n = 6114) cases; estimated daily reproduction number ($R_t$) | Incidence increased initially to peak of ~400 probable and 150 confirmed cases/day on second and third days of closure, then declined gradually over the closure period. $R_t$ declined from ~1.6 before and during the closure, crossing 1 within 2 days of closure and remaining <1 thereafter. |
| Echevarria-Zuno et al (2009) [59] | Outbreak report | National population of Mexico, April – July 2009 | Response to outbreak; no mention of antiviral prophylaxis | Approx two weeks; entire education system (including nurseries and universities) initially in Mexico City and Mexico State from 23 April, then nationwide from 27 April [60]. Universities and high schools reopened 4-5 days before elementary schools [58]. | Schools closed early in growth phase of epidemic. | ILI reported through active surveillance of inpatients and outpatients | Epidemic continued while schools were closed and peaked ~1 week after closure; increase in cases over three days after reopening of universities and high schools, but not following subsequent reopening of elementary schools. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Lajous et al (2010) [61] | Outbreak report | 56,551 respondents to a text message survey, Mexico, April 2009 | Both planned closure and a response to the outbreak | Planned holiday lasted 1 week; reactive closure lasted at least one week (schools were still closed at the end of the time period presented) | Planned closure occurred in the early stages of the outbreak before national surveillance indicated an increase in the number of cases but case numbers from survey data were declining. Reactive closure occurred during the increase in national case numbers. | ILI in survey respondents; suspected or confirmed H1N1 from national surveillance | Planned closure was followed by a slight decrease in case numbers reported through national surveillance, but this increased before schools reopened. National surveillance data peaked ~3 days after the reactive school closure and then declined through the rest of the closure period. Survey data were not obviously affected by school closure, although the proportion of reported cases which prevented respondents working declined during both closure periods. |
| Gomez et al (2009) [62] | Outbreak report | National population of Peru, May – September 2009 | Appears to be reactive, but unclear; some use of prophylactic oseltamivir | 3 weeks, all schools nationwide | One week after peak week | Number of pneumonia cases in 5-59 year olds in Lima and Callao; number of severe acute respiratory infections nationally | Pneumonia cases decreased from peak week ~130 cases following closure to ~40 cases and showed slight resurgence to just below 60 cases when schools re-opened; effect on other severe respiratory infections difficult to assess as date of closure is unclear. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Tinoco et al (2009) [63] | Prospective cohort study | 1747 individuals in 343 randomly selected households, San Juan de Miraflores District, Lima, Peru, May – August 2009 | Unclear | ~3 weeks, presumably all schools | After peak | Influenza-like illness counts by causative organism (H1N1 or other); age-specific rates of confirmed H1N1v | Number of ILI cases (and confirmed H1N1) decreased throughout closure period, from 54 (39 H1N1) the preceding week to 29 (19), 12 (6) and 6 (3) in each subsequent week; rates of confirmed H1N1 reached zero in week following closure in all age groups except 50-59 year olds. |
| Lessler et al (2009) [64] | Outbreak report | 1453 students (aged 14-19) and staff at a New York City high school, April – May 2009 | Response to outbreak | 9 days, one school | After peak | Confirmed H1N1 influenza or self-reported ILI | Incidence already declining when school was closed, continued to decline through closure period. No data presented for period following re-opening. |
| Miller et al (2010) [65] | Survey of schoolchildren regarding behaviour during reactive school closure | Private girls' school in Boston, USA; 63 of 176 children in grades 5-8 and 188 of 240 in grades 9-12. | Response to outbreak / high levels of absenteeism | One week | 4 days after peak | Fever in pupils with ILI, and absenteeism, in upper and lower school separately | Upper and lower schools each had one case of fever on the first day of closure and continued to have 0 or 1 case per day throughout the closure period; no apparent increase on reopening. Absenteeism in both schools was considerably higher before closure than after reopening. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Janjua et al (2010) [66] | Telephone survey of households of children enrolled in any of the six schools in the community, primarily aimed at conducting a case-control study of the effect of vaccination against seasonal influenza on risk of infection with pandemic H1N1. | Elementary school and surrounding community, British Colombia, Canada, April – May 2009. | Response to outbreak in one elementary school | 9 days | Outbreak peaked on the first day of school closure | ILI (n = 92) in 1092 participants from households of children attending any school in the community | Daily number of cases declined during school closure (from 10 cases on the first day to 1 case on the final day), increasing to 5 cases on the day of reopening. Case numbers ranged from 0-3 per day for the remainder of the study period. |
| Marchbanks et al (2011) [67] | Outbreak report | 388 of 456 pupils at an elementary school in Pennsylvania, USA, and 957 household contacts, May 2009. | Response to outbreak | 7 days | ILI peaked two days before school closure. | ILI (93 pupils and 74 contacts): subjective fever with cough and / or sore throat. | Incidence increased on second day of closure and then declined; very slight increase on reopening (although absenteeism returned to normal). No cases occurredin the 4th grade during closure or after reopening. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Cauchemez et al (2011) [68] | More detailed modelling analysis of outbreak described in Marchbanks et al [67] | Same school as Marchbanks et al [67], but using data from 27 April to 30 May 2009 from 370 pupils and 899 household contacts. | As Marchbanks et al [67] | As Marchbanks et al [67] | ARI epidemic curve peaked 2 and 3 days before closure. | Acute respiratory infection (at least two of fever, cough, sore throat, runny nose) in children attending the affected school (stratified by grade) and their household contacts (stratified into adults and children).129 cases in pupils and 141 in household contacts. | Incidence increased on the second day of closure but then declined; slight increase on reopening. Statistical analysis found no evidence of an effect of closure on the transmission rate among pupils (30% reduction, 95% credible interval 62% decrease to 22% increase). Reproduction number was also similar (0.3) during the week of closure and the following week. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Janusz et al (2011) [69] | Outbreak report and community-based survey. Community survey collected data from 240 of 711 households approached (comprising 644 individuals). | A community associated with a school which experienced an outbreak, Chicago, USA, April – May 2009. | Response to outbreak. | 7 days; one of the five elementary schools in the community closed. | Approximately one third of ILI cases reported through the survey had occurred before school closure (0-3 per day). Only 4 laboratory-confirmed cases had been reported to the Department of Health before closure. | ILI (fever with cough and / or sore throat, n = 37) in the survey; laboratory confirmed H1N1 infection reported to Chicago Department of Public Health (n = 43) based on date of specimen collection, although the peak based on date of onset occurred 3 days before closure. | In the community survey, maximum of 3 cases per day before and during closure; no increase when school reopened. None of the cases reported through this survey were linked to the affected school.<br><br>Laboratory reports peaked on the first day of closure, generally declined during closure and remained low after reopening; however, testing recommendations changed on the second day of closure. |
| Cohen et al (2011) [70] | Outbreak report | Pupils at a school in Chicago which closed due to the outbreak, and their household contacts (170 households, of 609 eligible, provided data), April – May 2009. | Response to outbreak. | 1 week. | Highest numbers of cases were reported on the two days before closure. | Acute respiratory illness (one or more of fever, cough, sore throat, rhinorrhoea or nasal congestion, n = 58). | Case numbers were lower on the first day of closure than on the two previous days, increased during closure and then declined. Few cases were reported after school reopened. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
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| Loustalot et al (2011) [71] | Questionnaire survey / assessment of household secondary attack rate and use of non-pharmaceutical interventions. | 668 households (2772 individuals) of 1716 approached, with children attending a closed high school in San Antonio, Texas, March – June 2009. | Response to outbreak | 9 days | Peak occurred 8 days before school closure | ILI in household members reported by one adult household member, stratified into index cases (students attending the affected school, n = 78) and secondary cases (n = 21) | Incidence remained low during closure; no cases reported on the final four days of closure. 1-2 cases per day after school reopened. |
| Chowell et al (2011a) [72] | Epidemiological and modelling analysis of outbreak data | 107 million individuals registered with a Mexican private medical system, April – December 2009 | Response to outbreak, and a later planned summer holiday. | Reactive closure lasted from 24 April to 5 May; summer holiday lasted ~7 weeks; all schools nationally were closed. | Reactive closure occurred early in the first wave of the outbreak (together with other interventions); summer holiday followed a plateau in the number of confirmed cases. | Confirmed pandemic H1N1 cases or ratio of number of cases in students (aged 5-20 years) to number of cases in other age groups. | Reactive closure appeared to slow epidemic growth, which resumed when interventions were lifted. Incidence was reasonably constant in all ages during the summer holiday but declined amongst students; cases amongst students and others increased when schools reopened (as did the ratio of student to non-student cases). |
| Herrera-Valdez et al (2011) [73] | Modelling analysis, including estimation of change in contact rate during school closure period. | National population of Mexico, April – November 2009 | One reactive closure and a subsequent planned holiday | Reactive closure lasted ~2 weeks; holiday lasted ~2 months. | Schools closed reactively early in growth phase; holiday started close to the peak of the second wave. | Confirmed pandemic H1N1 cases; model estimates of contact rate. | Confirmed cases occurred in three waves corresponding to closing and reopening of schools. Estimated contact rates appeared to be reduced by ~80% during school closure periods. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Chowell et al (2011b) [74] | Epidemiological / spatial analysis of outbreak data | General population of Peru, May – December 2009 | Planned school holiday moved forward by two weeks | Three weeks, all schools in the country | After the peak in daily national data; same week as peak in weekly data stratified into students and others. | Confirmed pandemic H1N1 cases or ratio of number of cases in students (aged 5-20 years) to number of cases in other age groups. | Number of cases in whole population, students and others declined throughout closure period; no clear increase on reopening. Ratio of student to non-student cases had already peaked, but declined during closure and increased afterwards. |
| Monto et al (1970) [75] | Non-randomised community trial of pandemic vaccine | All schoolchildren in Tecumseh (approx 3680) and Adrian (number not stated), Michigan, November 1968 – January 1969. 86% of children and a small number of adults in Tecumseh were vaccinated against the pandemic strain. Pandemic vaccine was not used in Adrian. | Christmas holiday | Two weeks, presumably all schools | Peak absenteeism in Adrian occurred one week before closure; Tecumseh did not experience an extensive epidemic. | School absenteeism (all causes) | Absenteeism in Adrian was >14% on each of the four days before closure and was ~8% on the day of reopening. Tecumseh did not experience any clear peaks in absenteeism. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Bootsma and Ferguson (2007) [76] | Statistical / transmission modelling analysis of historical P&I mortality data | 23 US cities with data on timing of introduction of NPIs during 1918 influenza pandemic | Response to outbreaks; other social distancing measures also implemented | Approx 0-7 weeks, depending on city | Varied by city | Excess total or peak mortality in each city | Correlation between excess / peak mortality and timing of introduction of NPIs relative to progress of epidemic ($p<0.01$ in both cases). Lifting of NPIs allowed transmission to become established again |
| Hatchett et al (2007) [77] | Statistical analysis of historical P&I mortality data | 17 US cities, September – December 1918 | Response to outbreaks; other social distancing measures also implemented | Varied by city | Varied by city | Cumulative Excess P&I death rates (CEPID) | Cities which closed schools before CEPID reached 30/100,000 had a lower median peak weekly excess P&I death rate than those which did not ($p<0.01$) but there was no significant difference in median CEPID.<br>Closing schools at a higher CEPID was associated with higher peak P&I death rates (Spearman $\rho$ =0.54) but not with total P&I death rates. Second waves occurred only after lifting of NPIs. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Markel et al (2007) [78] | Statistical analysis of historical mortality data | 43 US cities, September 1918 – February 1919 | Response to outbreaks; other social distancing measures also implemented | Varied by city | Varied by city | Weekly excess P&I death rates | Not uniform across cities (but this could be related to the timing of the intervention). Earlier interventions correlated with increased time to epidemic peak (r = -0.74, p<0.001), reduced peak excess death rate (r = 0.31, p=0.02) and reduced total excess death rate (r = 0.37, p=0.008). Increased duration of intervention associated with reduced total excess death rate (r = -0.39, p=0.005). |
| Jordan et al (1919) [79] | Outbreak report | Elementary school (391 pupils aged 4-13 years) and high school (427 pupils aged 14-18 years) of University of Chicago, October – December 1918 | Planned Thanksgiving break | Four days (including weekend) | Both schools were closed for final three days of peak week and one day of the following week. | Clinical influenza (n = 97 in elementary school, n = 91 in high school) | Elementary school: incidence declined from 19 cases in peak week to 15 the following week, showed a second peak of 10 cases 3 weeks after the closure. High school: incidence decreased from 16 cases in peak week to 5 the following week, showed a second peak of 11 cases 2 weeks after the closure. |

| Study | Study design | Study population / Setting | Nature of closure | Duration of closure and schools affected | Timing of closure in relation to influenza circulation | Outcome measure | Association between school closure and outcome |
|---|---|---|---|---|---|---|---|
| Armstrong and Hopkins (1921) [80] | Outbreak report | Kelleys Island, Lake Erie, US, January – February 1920, population 689 (of whom 157 were schoolchildren) | Response to staff and student absenteeism during influenza outbreak | The single school (for both grammar and high school pupils) on the island remained closed "until the epidemic had subsided" | Epidemic began 24 January, school closed 30 January | Self-reported clinical influenza, based on checklist of symptoms ( n = 369) | Overall incidence peaked at 52 cases on day following closure. Cases in schoolchildren dipped on day of closure, peaked following day and declined thereafter. Cases in other groups dipped two days after closure, peaked the following day and then declined. |
| Winslow and Rogers (1920) [81] | Outbreak report | Connecticut, USA, September – December 1918 | Response to outbreak | Three cities in which schools remained open are cited and mortality rates compared descriptively with two cities in which schools were closed. Duration of closures not stated. | Not stated. | Deaths from pneumonia and influenza | Death rates were lower in the three cities in which schools remained open than in at least two cities in which they were closed. |

## Supplementary references

1. Briscoe JH. The protective effect of influenza vaccine in a mixed influenza A and B epidemic in a boys' boarding school. *J R Coll Gen Pract* 1977;27(166):28-31.
2. Davies JR, Grilli EA, Smith AJ, Hoskins TW. Prophylactic use of amantadine in a boarding school outbreak of influenza A. *J R Coll Gen Pract* 1988;38(313):346-8.
3. Grilli EA, Anderson MJ, Hoskins TW. Concurrent outbreaks of influenza and parvovirus B19 in a boys' boarding school. *Epidemiology and Infection* 1989;103(2):359-69.
4. Danis K, Fitzgerald M, Connell J, Conlon M, Murphy PG. Lessons from a pre-season influenza outbreak in a day school. *Commun Dis Public Health* 2004;7(3):179-83.
5. Miller DL, Lee JA. Influenza in Britain 1967-68. *Journal of Hygiene* 1969;67:559-72.
6. Cauchemez S, Valleron A-J, Boelle P-Y, Flahault A, Ferguson NM. Estimating the impact of school closure on influenza transmission from Sentinel data. *Nature* 2008;452(7188):750-4.
7. Olson JG. School absenteeism during an outbread of B/Hong Kong/5/72-like influenze virus in Taipei, Taiwan. *Southeast Asian J Trop Med Public Health* 1980;11(4):429-34.
8. Sonoguchi T, Naito H, Hara M. Cross-subtype protection in humans during sequential, overlapping, and/or concurrent epidemics caused by H3N2 and H1N1 influenza viruses. *Journal of Infectious Diseases* 1985;151(1):81-88.
9. Fujii H, Takahashi H, Ohyama T, Hattori K, Suzuki S. Evaluation of the school health surveillance system for influenza, Tokyo, 1999-2000. *Japanese Journal of Infectious Diseases* 2002;55(3):97-98.
10. Heymann A, Chodick G, Reichman B, Kokia E, Laufer J. Influence of school closure on the incidence of viral respiratory diseases among children and on health care utilization. *Pediatr Infect Dis J* 2004;23(7):675-7.
11. Heymann AD, Hoch I, Valinsky L, Kokia E, Steinberg DM. School closure may be effective in reducing transmission of respiratory viruses in the community. *Epidemiol Infect* 2009;137(10):1369-76.
12. Lo JY, Tsang TH, Leung YH, Yeung EY, Wu T, Lim WW. Respiratory infections during SARS outbreak, Hong Kong, 2003. *Emerg Infect Dis* 2005;11(11):1738-41.
13. Cowling BJ, Lau EHY, Lam CLH, Cheng CKY, Kovar J, Chan KH, et al. Effects of school closures, 2008 winter influenza season, Hong Kong. *Emerg Infect Dis* 2008;14(10):1660-2.
14. Cashman P, Massey P, Durrheim D, Islam F, Merritt T, Eastwood K. Pneumonia cluster in a boarding school--implications for influenza control. *Commun Dis Intell* 2007;31(3):296-8.
15. Shaw C, McLean M, McKenzie J. Other surveillance reports: influenza-like illness in Wellington schools 2005. *New Zealand Public Health Surveillance Report* 2006;4(2):4-6.
16. Leonida DDJ. Morbidity patterns reflected in a school health program during an influenza epidemic season. *Illinois Medical Journal* 1970;137(3):262-64.
17. Glass RI, Brann EA, Slade JD, Jones WE, Scally MJ, Craven RB, et al. Community-wide surveillance of influenza after outbreaks due to H3N2 (A/Victoria/75 and A/Texas/77) and H1N1 (A/USSR/77) influenza viruses, Mercer County, New Jersey, 1978. *Journal of Infectious Diseases* 1978;138(5):703-6.
18. Farley TA, St. Germain JM, Chamberlain LA, Krassner L. The impact of influenza vaccination on respiratory illness at a boarding School. *Journal of American College Health* 1992;41(3):127-31.

19. Louie JK, Schnurr DP, Guevara HF, Honarmand S, Cheung M, Cottam D, et al. Creating a Model Program for Influenza Surveillance in California. Results from the 2005-2006 Influenza Season. *American Journal of Preventive Medicine* 2007;33(4):353-57.
20. Johnson AJ, Moore ZS, Edelson PJ, Kinnane L, Davies M, Shay DK, et al. Household responses to school closure resulting from outbreak of influenza B, North Carolina. *Emerg Infect Dis* 2008;14(7):1024-30.
21. Rodriguez CV, Rietberg K, Baer A, Kwan-Gett T, Duchin J. Association between school closure and subsequent absenteeism during a seasonal influenza epidemic. *Epidemiology* 2009;20(6):787-92.
22. Wheeler CC, Erhart LM, Jehn ML. Effect of school closure on the incidence of influenza among school-age children in Arizona. *Public Health Rep* 2010;125(6):851-9.
23. Smith A, Coles S, Johnson S, Saldana L, Ihekweazu C, O'Moore E. An outbreak of influenza A(H1N1)v in a boarding school in South East England, May-June 2009. *Euro Surveill* 2009;14(27):9.
24. Health Protection Agency West Midlands H1N1v Investigation Team. Preliminary descriptive epidemiology of a large school outbreak of influenza A(H1N1)v in the West Midlands, United Kingdom, May 2009. *Euro Surveill* 2009;14(27).
25. Wallensten A, Oliver I, Lewis D, Harrison S. Compliance and side effects of prophylactic oseltamivir treatment in a school in South West England. *Euro Surveill* 2009;14(30):19285.
26. Calatayud L, Kurkela S, Neave PE, Brock A, Perkins S, Zuckerman M, et al. Pandemic (H1N1) 2009 virus outbreak in a school in London, April-May 2009: an observational study. *Epidemiol Infect* 2010;138(2):183-91.
27. Strong M, Burrows J, Stedman E, Redgrave P. Adverse drug effects following oseltamivir mass treatment and prophylaxis in a school outbreak of 2009 pandemic influenza A(H1N1) in June 2009, Sheffield, United Kingdom. *Euro Surveill* 2010;15(19):pii/19565.
28. Baguelin M, Hoek AJV, Jit M, Flasche S, White PJ, Edmunds WJ. Vaccination against pandemic influenza A/H1N1v in England: A real-time economic evaluation. *Vaccine* 2010;28(12):2370-84.
29. Guinard A, Grout L, Durand C, Schwoebel V. Outbreak of influenza A(H1N1)v without travel history in a school in the Toulouse district, France, June 2009. *Euro Surveill* 2009;14(27).
30. Carrillo-Santisteve P, Renard-Dubois S, Cheron G, Csaszar-Goutchkoff M, Lecuit M, Lortholary O, et al. 2009 pandemic influenza A(H1N1) outbreak in a complex of schools in Paris, France, June 2009. *Euro Surveill* 2010;15(25):24.
31. Poggensee G, Gilsdorf A, Buda S, Eckmanns T, Claus H, Altmann D, et al. The first wave of pandemic influenza (H1N1) 2009 in Germany: From initiation to acceleration. *BMC Infectious Diseases* 2010;10(155).
32. Birrell PJ, Ketsetzis G, Gay NJ, Cooper BS, Presanis AM, Harris RJ, et al. Bayesian modeling to unmask and predict influenza A/H1N1pdm dynamics in London. *Proceedings of the National Academy of Sciences of the United States of America* 2011;108(45):18238-43.
33. Evans B, Charlett A, Powers C, McLean E, Zhao H, Bermingham A, et al. Has estimation of numbers of cases of pandemic influenza H1N1 in England in 2009 provided a useful measure of the occurrence of disease? *Influenza and other Respiratory Viruses* 2011;5(6):e504-e12.
34. Smith S, Smith GE, Olowokure B, Ibbotson S, Foord D, Maguire H, et al. Early spread of the 2009 infuenza A(H1N1) pandemic in the United Kingdom - use of local syndromic data, May-August 2009. *Eurosurveillance* 2011;16(3).

35. Flasche S, Hens N, Boëlle P-Y, Mossong J, van Ballegooijen WM, Nunes B, et al. Different transmission patterns in the early stages of the influenza A(H1N1)v pandemic: A comparative analysis of 12 European countries. *Epidemics* 2011;3(2):125-33.
36. Van Gageldonk-Lafeber AB, Hooiveld M, Meijer A, Donker GA, Veldman-Ariesen MJ, van der Hoek W, et al. The relative clinical impact of 2009 pandemic influenza A (H1N1) in the community compared to seasonal influenza in the Netherlands was most marked among 5-14year olds. *Influenza and other Respiratory Viruses* 2011;5(6):e513-e20.
37. Merler S, Ajelli M, Pugliese A, Ferguson NM. Determinants of the spatiotemporal dynamics of the 2009 H1N1 pandemic in europe: Implications for real-time modelling. *PLoS Computational Biology* 2011;7(9).
38. Petrovic V, Seguljev Z, Cosic G, Ristic M, Nedeljkovic J, Dragnic N, et al. Overview of the winter wave of 2009 pandemic influenza A(H1N1)v in Vojvodina, Serbia. *Croatian Medical Journal* 2011;52(2):141-50.
39. Human infection with new influenza A (H1N1) virus: clinical observations from a school-associated outbreak in Kobe, Japan, May 2009. *Wkly Epidemiol Rec* 2009;84(24):237-44.
40. Nishiura H, Castillo-Chavez C, Safan M, Chowell G. Transmission potential of the new influenza A(H1N1) virus and its age-specificity in Japan. *Euro Surveill* 2009;14(22):4.
41. Shimada T, Gu Y, Kamiya H, Komiya N, Odaira F, Sunagawa T, et al. Epidemiology of influenza A(H1N1)v virus infection in Japan, May-June 2009. *Euro Surveill* 2009;14(24).
42. Kawaguchi R, Miyazono M, Noda T, Takayama Y, Sasai Y, Iso H. Influenza (H1N1) 2009 outbreak and school closure, Osaka Prefecture, Japan. *Emerg Infect Dis* 2009;15(10):1685.
43. Chieochansin T, Makkoch J, Suwannakarn K, Payungporn S, Poovorawan Y. Novel H1N1 2009 influenza virus infection in Bangkok, Thailand:Effects of school closures. *Asian Biomedicine* 2009;3(5):469-75.
44. Wu JT, Cowling BJ, Lau EH, Ip DK, Ho LM, Tsang T, et al. School closure and mitigation of pandemic (H1N1) 2009, Hong Kong. *Emerg Infect Dis* 2010;16(3):538-41.
45. Cowling BJ, Lau MSY, Ho LM, Chuang SK, Tsang T, Liu SH, et al. The effective reproduction number of pandemic influenza: Prospective estimation. *Epidemiology* 2010;21(6):842-46.
46. Hsueh P-R, Lee P-I, Hsiang Chiu A-W, Yen M-Y. Pandemic (H1N1) 2009 vaccination and class suspensions after outbreaks, Taipei City, Taiwan. *Emerg Infect Dis* 2010;16(8):1309-11.
47. Wu J, Xu F, Lu L, Lu M, Miao L, Gao T, et al. Safety and effectiveness of a 2009 H1N1 vaccine in Beijing. *New England Journal of Medicine* 2010;363(25):2416-23.
48. Huai Y, Lin J, Varma JK, Peng Z, He J, Cheng C, et al. A primary school outbreak of pandemic 2009 influenza A (H1N1) in China. *Influenza other respi* 2010;4(5):259-66.
49. Engelhard D, Bromberg M, Averbuch D, Tenenbaum A, Goldmann D, Kunin M, et al. Increased extent of and risk factors for pandemic (H1N1) 2009 and seasonal infl uenza among children, Israel. *Emerging Infectious Diseases* 2011;17(9):1740-43.
50. Leung YH, Li MP, Chuang SK. A school outbreak of pandemic (H1N1) 2009 infection: assessment of secondary household transmission and the protective role of oseltamivir. *Epidemiol Infect* 2011;139(1):41-4.

51. Uchida M, Tsukahara T, Kaneko M, Washizuka S, Kawa S. Swine-origin influenza a outbreak 2009 at Shinshu University, Japan. *BMC Public Health* 2011;11:79.
52. Rajatonirina S, Heraud J-M, Randrianasolo L, Razanajatovo N, Ramandimbisoa T, Ratsitorahina M, et al. Pandemic influenza A(H1N1) 2009 virus outbreak among boarding school pupils in Madagascar: compliance and adverse effects of prophylactic oseltamivir treatment. *J* 2011;5(3):156-62.
53. Caley P, Philp DJ, McCracken K. Quantifying social distancing arising from pandemic influenza. *Journal of the Royal Society Interface* 2008;5(23):631-9.
54. Baker MG, Wilson N, Huang QS, Paine S, Lopez L, Bandaranayake D, et al. Pandemic influenza A(H1N1)v in New Zealand: the experience from April to August 2009. *Euro Surveill* 2009;14(34).
55. Hall RJ, Peacey MP, Ralston JC, Bocacao J, Ziki M, Gunn W, et al. Pandemic influenza A(H1N1)v viruses currently circulating in New Zealand are sensitive to oseltamivir. *Euro Surveill* 2009;14(30):19282.
56. Effler PV, Carcione D, Giele C, Dowse GK, Goggin L, Mak DB. Household responses to pandemic (H1N1) 2009-related school closures, Perth, Western Australia. *Emerg Infect Dis* 2010;16(2):205-11.
57. Paine S, Mercer GN, Kelly PM, Bandaranayake D, Baker MG, Huang QS, et al. Transmissibility of 2009 pandemic influenza A(H1N1) in New Zealand: effective reproduction number and influence of age, ethnicity and importations. *Euro Surveill* 2010;15(24).
58. Cruz-Pacheco G, Duran L, Esteva L, Minzoni A, Lopez-Cervantes M, Panayotaros P, et al. Modelling of the influenza A(H1N1)v outbreak in Mexico City, April-May 2009, with control sanitary measures. *Euro Surveill* 2009;14(26).
59. Echevarria-Zuno S, Mejia-Arangure JM, Mar-Obeso AJ, Grajales-Muniz C, Robles-Perez E, Gonzalez-Leon M, et al. Infection and death from influenza A H1N1 virus in Mexico: a retrospective analysis. *Lancet* 2009.
60. Stern AM, Markel H. What Mexico taught the world about pandemic influenza preparedness and community mitigation strategies. *Jama* 2009;302(11):1221-2.
61. Lajous M, Danon L, Lopez-Ridaura R, Astley CM, Miller JC, Dowell SF, et al. Mobile messaging as surveillance tool during pandemic (H1N1) 2009, Mexico. *Emerg Infect Dis* 2010;16(9):1488-9.
62. Gomez J, Munayco C, Arrasco J, Suarez L, Laguna-Torres V, Aguilar P, et al. Pandemic influenza in a southern hemisphere setting: the experience in Peru from May to September, 2009. *Euro Surveill* 2009;14(42).
63. Tinoco Y, Razuri H, Ortiz EJ, Gomez J, Widdowson MA, Uyeki T, et al. Preliminary population-based epidemiological and clinical data on 2009 pandemic H1N1 influenza A (pH1N1) from Lima, Peru. *Influenza Other Respi Viruses* 2009;3(6):253-6.
64. Lessler J, Reich NG, Cummings DAT, New York City Department of H, Mental Hygiene Swine Influenza Investigation T, Nair HP, et al. Outbreak of 2009 pandemic influenza A (H1N1) at a New York City school. *N Engl J Med* 2009;361(27):2628-36.
65. Miller JC, Danon L, O'Hagan JJ, Goldstein E, Lajous M, Lipsitch M. Student behavior during a school closure caused by pandemic influenza A/H1N1. *PLoS ONE* 2010;5(5):e10425.
66. Janjua NZ, Skowronski DM, Hottes TS, Osei W, Adams E, Petric M, et al. Seasonal influenza vaccine and increased risk of pandemic A/H1N1-related illness: First detection of the association in British Columbia, Canada. *Clinical Infectious Diseases* 2010;51(9):1017-27.

67. Marchbanks TL, Bhattarai A, Fagan RP, Ostroff S, Sodha SV, Moll ME, et al. An outbreak of 2009 pandemic influenza A (H1N1) virus infection in an elementary school in Pennsylvania. *Clin Infect Dis* 2011;52 Suppl 1:S154-60.
68. Cauchemez S, Bhattarai A, Marchbanks TL, Fagan RP, Ostroff S, Ferguson NM, et al. Role of social networks in shaping disease transmission during a community outbreak of 2009 H1N1 pandemic influenza. *Proc Natl Acad Sci U S A* 2011;108(7):2825-30.
69. Janusz KB, Cortes JE, Serdarevic F, Jones RC, Jones JD, Ritger KA, et al. Influenza-like illness in a community surrounding a school-based outbreak of 2009 pandemic influenza A (H1N1) virus-Chicago, Illinois, 2009. *Clin Infect Dis* 2011;52 Suppl 1:S94-101.
70. Cohen NJ, Callahan DB, Gonzalez V, Balaban V, Wang RT, Pordell P, et al. Respiratory illness in households of school-dismissed students during pandemic (H1N1) 2009. *Emerging Infectious Diseases* 2011;17(9):1756-57.
71. Loustalot F, Silk BJ, Gaither A, Shim T, Lamias M, Dawood F, et al. Household transmission of 2009 pandemic influenza A (H1N1) and nonpharmaceutical interventions among households of high school students in San Antonio, Texas. *Clin Infect Dis* 2011;52 Suppl 1:S146-53.
72. Chowell G, Echevarria-Zuno S, Viboud C, Simonsen L, Tamerius J, Miller MA, et al. Characterizing the epidemiology of the 2009 influenza A/H1N1 pandemic in Mexico. *PLoS Med* 2011;8(5):e1000436.
73. Herrera-Valdez MA, Cruz-Aponte M, Castillo-Chavez C. Multiple outbreaks for the same pandemic: Local transportation and social distancing explain the different "Waves" of A-H1N1PDM cases observed in Mexico during 2009. *Mathematical Biosciences and Engineering* 2011;8(1):21-48.
74. Chowell G, Viboud C, Munayco CV, Gomez J, Simonsen L, Miller MA, et al. Spatial and temporal characteristics of the 2009 A/H1N1 influenza pandemic in Peru. *PLoS ONE* 2011;6(6):e21287.
75. Monto AS, Davenport FM, Napier JA, Francis Jr T. Modification of an outbreak of influenza in tecumseh, michigan by vaccination of schookhildren. *J.Infect.Dis* 1970;122(1-2):328-32.
76. Bootsma MC, Ferguson NM. The effect of public health measures on the 1918 influenza pandemic in U.S. cities. *Proc Natl Acad Sci U S A* 2007;104(18):7588-93.
77. Hatchett RJ, Mecher CE, Lipsitch M. Public health interventions and epidemic intensity during the 1918 influenza pandemic. *Proc Natl Acad Sci U S A* 2007;104(18):7582-7.
78. Markel H, Lipman HB, Navarro JA, Sloan A, Michalsen JR, Stern AM, et al. Nonpharmaceutical interventions implemented by US cities during the 1918-1919 influenza pandemic.[Erratum appears in JAMA. 2007 Nov 21;298(19):2264]. *Jama* 2007;298(6):644-54.
79. Jordan EO, Redd DB, Fink EB. Influenza in three Chicago groups. *Public Health Rep* 1919;34(28):1528-45.
80. Armstrong C, Hopkins R. An epidemiological study of the 1920 epidemic of influenza in an isolated rural community. *Public Health Reports* 1921;36(29):1671-702.
81. Winslow C-EA, Rogers JF. Statistics of the 1918 Epidemic of Influenza in Connecticut: With a consideration of the factors which influenced the prevalence of this disease in various communities *J Infect Dis* 1920;26(3):185-216.

# PRISMA 2009 Checklist

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 3 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | NA |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | NA |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 3-4 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 3-4 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | Appendix, p1 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 4 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 4 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 29 (Box 1) |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | NA |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 4 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | NA |

# PRISMA 2009 Checklist



| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | NA |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | NA |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 5, Figure 1 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | Appendix Tables 1 and 2 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | NA |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | NA |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | NA |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | NA |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | NA |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 12 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 12-16 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 16 |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 19 |

*From:* Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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